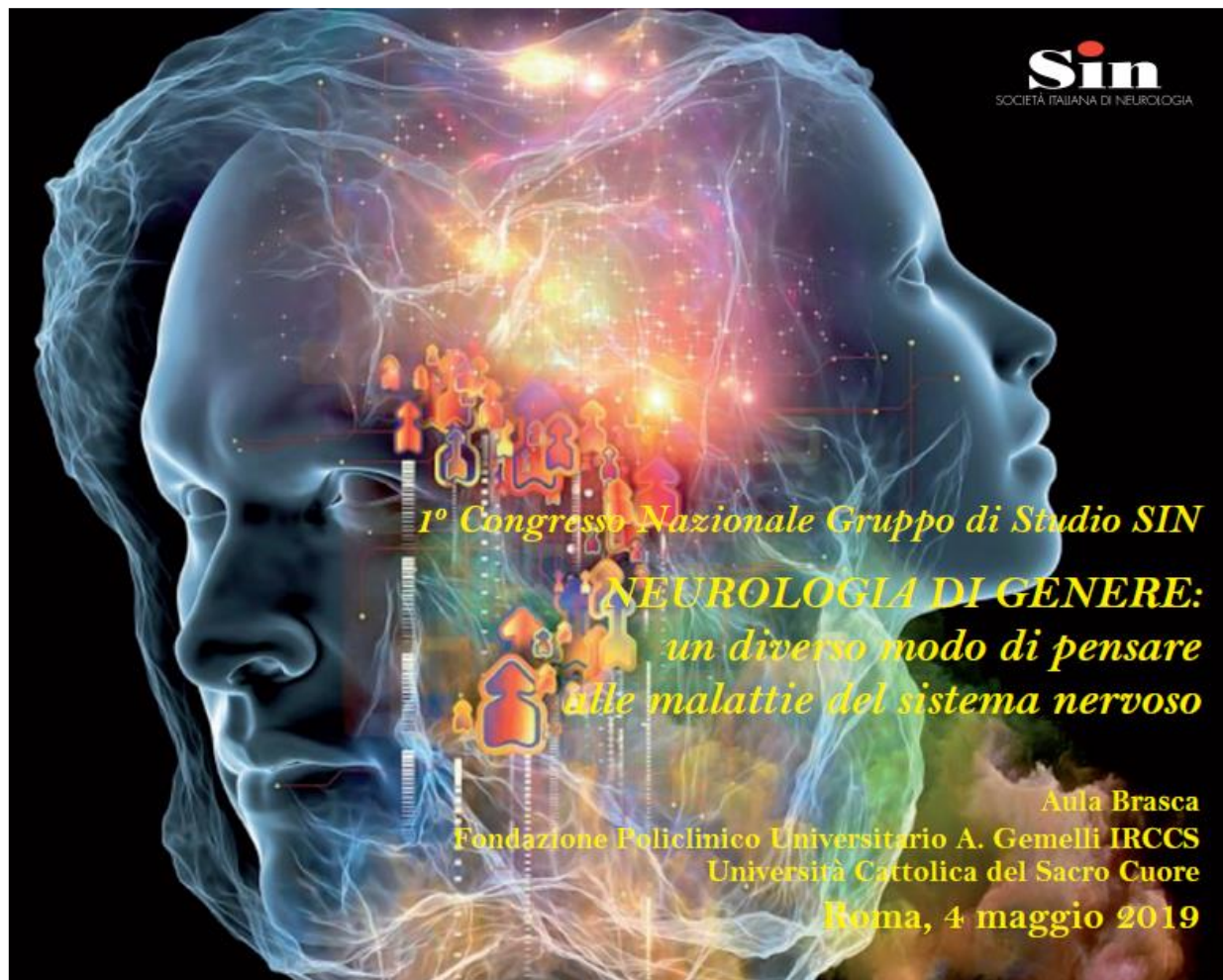




Sin
SOCIETÀ ITALIANA DI NEUROLOGIA

1° Congresso Nazionale Gruppo di Studio SIN

NEUROLOGIA DI GENERE:
*un diverso modo di pensare
alle malattie del sistema nervoso*

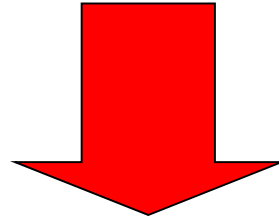
Aula Brasca
Fondazione Policlinico Universitario A. Gemelli IRCCS
Università Cattolica del Sacro Cuore
Roma, 4 maggio 2019

1950-1992: "Women's Health" Emerges

- Emergence of feminism.
- Public Health Service Task Force on Women's Health: 1985.
- NIH mandates inclusion of women in clinical research. 1990-1992.
- Women's Health Equity Acts establish the Office of Research on Women's Health at the NIH: 1992.
- FDA mandates inclusion of women in trials of new drugs wherever appropriate: 1997



“WOMEN IN DEVELOPMENT”



“GENDER AND DEVELOPMENT”

Medical Woman International Association (2002)

<https://mwia.net/wp-content/uploads/2013/07/TrainingManualonGenderMainstreaminginHealth.pdf>



A Gender Gap in Autoimmunity

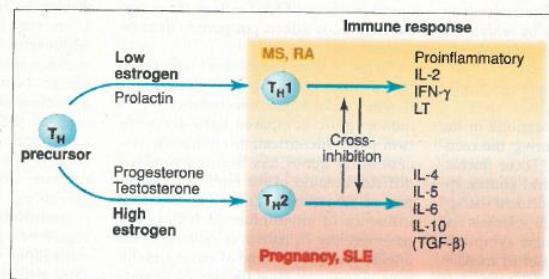
Caroline C. Whitacre, Stephen C. Reingold, Patricia A. O'Looney, and the Task Force on Gender, Multiple Sclerosis and Autoimmunity

Autoimmune diseases—such as multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and thyroiditis—affect over 8.5 million people in the United States. Of these, a disproportionate number (about 6.7 million) are women (1). In multiple sclerosis and rheumatoid arthritis, the female to male ratio is between 2:1 and 3:1, whereas in lupus the distribution is more skewed, with nine times as many women affected as men (2). The precise reasons for this gender bias are unclear.

To promote further understanding of the basis for gender differences in autoimmune disease, a task force of clinical and basic scientists was convened by the U.S. National Multiple Sclerosis Society. The task force summarized what is currently known about sex differences in autoimmunity and developed a research agenda, ranking five areas as priorities for future investigation. In addition, they formulated a policy to encourage collection and examination of data in a gender-stratified manner [see (3) for full report].

Distinct immune environments in males and females underlie many of the sex differences in autoimmunity. These environments are established by the cytokines released by immune cells, particularly T helper (T_H) lymphocytes. These cells respond to an immune challenge in one of two ways: T_H1 lymphocytes secrete interleukin-2 (IL-2), interferon- γ (IFN- γ), and

lymphotoxin, establishing a proinflammatory environment, whereas T_H2 lymphocytes secrete IL-4, IL-5, IL-6, IL-10, and transforming growth factor- β (TGF- β), which promote antibody production (see the figure). Both sets of lymphocytes exert cross-regulatory influences on each other. Females are more likely to develop a T_H1 response after challenge with an infectious



Hormonal influences. T helper 1 (T_H1) cells secrete proinflammatory cytokines and promote cell-mediated immune responses, whereas T_H2 cells trigger antibody production. In multiple sclerosis (MS) and rheumatoid arthritis (RA), there are features characteristic of a T_H1 immune response directed against autoantigens in the central nervous system and joints, respectively. Pregnancy and systemic lupus erythematosus (SLE) favor a T_H2 environment. Sex hormones (such as progesterone) that promote the development of a T_H2 response antagonize the emergence of T_H1 cells. This may explain why in multiple sclerosis and rheumatoid arthritis disease symptoms improve during pregnancy, whereas in lupus, they do not.

agent or antigen, except during pregnancy when a T_H2 environment prevails. This is evident in experimental infections of animals where viruses such as vesicular stomatitis virus or herpesvirus, which require an inflammatory response for resolution, cause milder disease in females. However, lymphocytic choriomeningitis virus, which invades the central nervous system and elicits a T_H1 response, causes more neuropathology in females. Whether humans show similar gender differences in susceptibility to infectious diseases and their outcome remains to be seen.

The degree of immune response also differs between men and women. Immune responses tend to be more vigorous in females, resulting in greater antibody production and increased cell-mediated immunity after immunization. Important questions remain about the differences between males and females in production and secretion of immunomodulatory me-

diators such as TGF- β , interferons, prostaglandins, and individual T_H1 and T_H2 cytokines.

Direct comparisons of males and females to determine specific differences in the innate and adaptive immune responses is crucial. Such comparisons should encompass all phases of lymphocyte development, including early differentiation, tolerance, and senescence. Although such studies are feasible in animals, direct comparisons in humans pose unique problems—for example, obtaining sufficient enrollment of males with lupus. To carry out such studies, large-scale international cooperation between urban medical centers will be necessary.

The predominance of autoimmune disease among women suggests that sex hormones may modulate susceptibility. Most attention has been directed toward the sex steroids—estrogens, progesterone, and testosterone—that are produced in the ovary and testis. Estrogen's effects on normal immune responses and in autoimmune disease appeared to be contradictory, until it was realized that this hormone has biphasic dose effects, with lower levels enhancing and higher levels (such as those in pregnancy) inhibiting specific immune activities. The recent identification of a second estrogen receptor has prompted new areas of investigation. For example, which estrogen receptor is expressed by different immune cells? What do the two receptors do, and are there gender differences? How is receptor expression regulated? Progesterone promotes the development of human T_H2 cells and so antagonizes the emergence of the T_H1 response (see the figure). Similarly, testosterone has anti-inflammatory properties and exerts immunosuppressive effects in several animal models of autoimmunity.

The sexually dimorphic pituitary hormones, prolactin and growth hormone, as well as liver-derived insulin-like growth factor-1, also affect autoimmune disease. Women have higher levels of these hormones than men. Prolactin and growth hormone enhance autoimmunity, whereas insulin-like growth factor-1 promotes the recovery and repair of injured neural tis-

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INSTITUTE OF MEDICINE

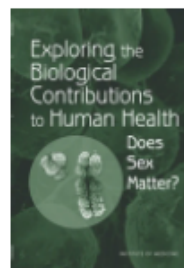
Shaping the Future for Health

EXPLORING THE BIOLOGICAL CONTRIBUTIONS TO HUMAN HEALTH: DOES SEX MATTER?

Over the past decade new discoveries in basic human biology have made it increasingly apparent that many normal physiological functions—and, in many cases, pathological functions—are influenced either directly or indirectly by sex-based differences in biology.

This realization, however, has been slow in coming. Considerable attention has focused on differences and similarities between females and males at the *societal* level by researchers evaluating how individual behaviors, lifestyles, and surroundings affect one's biological development and health. Similarly, at the level of the *whole organism* clinicians and applied researchers have investigated the component organs and systems of humans. However, scientists have paid much less attention to the direct study of these differences at the basic *cellular* and *molecular* levels. Where data are available, they have often been a by-product of other areas of research. Historically, the research community assumed that beyond the reproductive system, such differences do not exist or are not relevant. Still, scientific evidence of the importance of sex differences throughout the life span abounds.

Although an individual can be characterized initially by the presence of particular reproductive organs, sex differences encompass much more than that. Evidence suggests that the distinct anatomy and physiology that develop as a result of having been dealt two X chromosomes (XX) or an X chromosome and a Y chromosome (XY) at fertilization can have a much broader influence on an individual's health than was previously thought. While it is anatomically obvious why only males develop prostate cancer and only females get ovarian cancer, it is not at all obvious why, for example, females are more likely than males to recover language ability after suffering a left-hemisphere stroke or why females have a far greater risk than males of developing life-threatening ventricular arrhythmias in response to a variety of potassium channel-blocking drugs.



Sex refers to the classification of living things, generally as male or female according to their reproductive organs and functions assigned by chromosomal complement.

Gender refers to a person's self-representation as male or female, or how that person is responded to by social institutions based on the individual's gender presentation. Gender is rooted in biology and shaped by environment and experience.

Summary of Barriers to Progress in Research on Sex Differences

Terminology

- There is inconsistent and often confusing use of the terms *sex* and *gender* in the scientific literature and popular press.

Research Tools and Resources

- The conduct of research on sex differences and longitudinal research may require more complex studies and additional resources.
- Information on sex differences can be difficult to glean from the published literature.
 - Useful information on the sex of origin of cell and tissue culture material is often lacking in the literature.
 - There is a lack of data from longitudinal studies encompassing different diseases, disorders, and conditions across the life span.
 - There is a lack of consideration of hormonal variability.

Interdisciplinary and Collaborative Research

- The application of federal regulations is not uniform.
- Opportunities for interdisciplinary collaboration have been underused.

Non-Health-Related Implications of Research on Sex Differences in Health

- There is a lack of awareness that the consequences of genetics and physiology may be amenable to change.
- The finding of sex differences can lead to discriminatory practices.

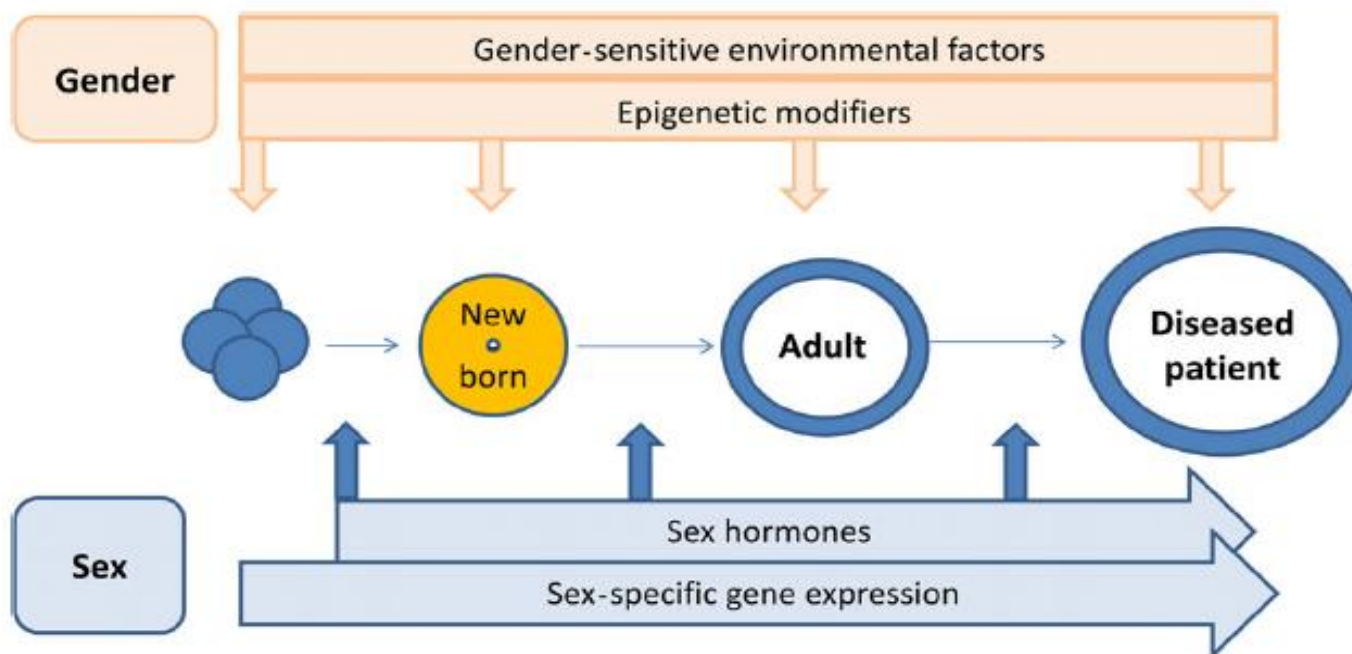
- **Genere**: insieme dei tratti di personalità, attitudini, sentimenti, valori, comportamenti e attività che la società attribuisce differenziatamente ai due sessi; è un costrutto sociale che varia da società a società e nel tempo
- **Sesso**: è una descrizione biologica, genotipica o fenotipica
- **Sessualità**: capacità di desiderio sessuale e della sua espressione
- Sesso e genere sono interattivi
- **Ruoli sessuali**: i particolari ruoli economici, sociali e le responsabilità considerate appropriate per donne e uomini in un determinato contesto sociale

- Nella ricerca il termine **sex** si riferisce ad una *variabile dicotomica* (femmina o maschio) in base ad aspetti anatomici (organi riproduttivi o cromosomi), in contrasto il **gender** è più spesso visto come una *variabile continua*. Il genere varia da esclusivamente femminile a esclusivamente maschile, con la possibilità che la maggior parte degli individui si collochi in un punto intermedio tra i due estremi
- Il genere può influenzare o confondere studi che valutano differenze di sesso

Gender in cardiovascular diseases: impact on clinical manifestations, management, and outcomes

The EUGenMed[†], Cardiovascular Clinical Study Group, Vera Regitz-Zagrosek^{1,2,3*}, Sabine Oertelt-Prigione^{1,2,3}, Eva Prescott⁴, Flavia Franconi^{2,5}, Eva Gerds⁶, Anna Foryst-Ludwig^{3,7}, Angela H.E.M. Maas⁸, Alexandra Kautzky-Willer^{2,9}, Dorit Knappe-Wegner^{2,10}, Ulrich Kintscher^{3,7}, Karl Heinz Ladwig¹¹, Karin Schenck-Gustafsson^{2,12}, and Verena Stangl^{3,13}

[†]Members of Cardiovascular Medicine, Center for Cardiovascular Research, Charité – Universitätsmedizin Berlin, University of Medicine, Berlin, Germany; ¹Charité – Universitätsmedizin Berlin, University of Medicine, Berlin, Germany; ²German Heart Research Network, Berlin, Germany; ³German Heart Research Network, Berlin, Germany; ⁴University of Gothenburg, Gothenburg, Sweden; ⁵University of Padua, Padua, Italy; ⁶University of Cologne, Cologne, Germany; ⁷University of Bonn, Bonn, Germany; ⁸University of Amsterdam, Amsterdam, The Netherlands; ⁹University of Vienna, Vienna, Austria; ¹⁰University of Bonn, Bonn, Germany; ¹¹University of Bonn, Bonn, Germany; ¹²University of Gothenburg, Gothenburg, Sweden; ¹³University of Bonn, Bonn, Germany



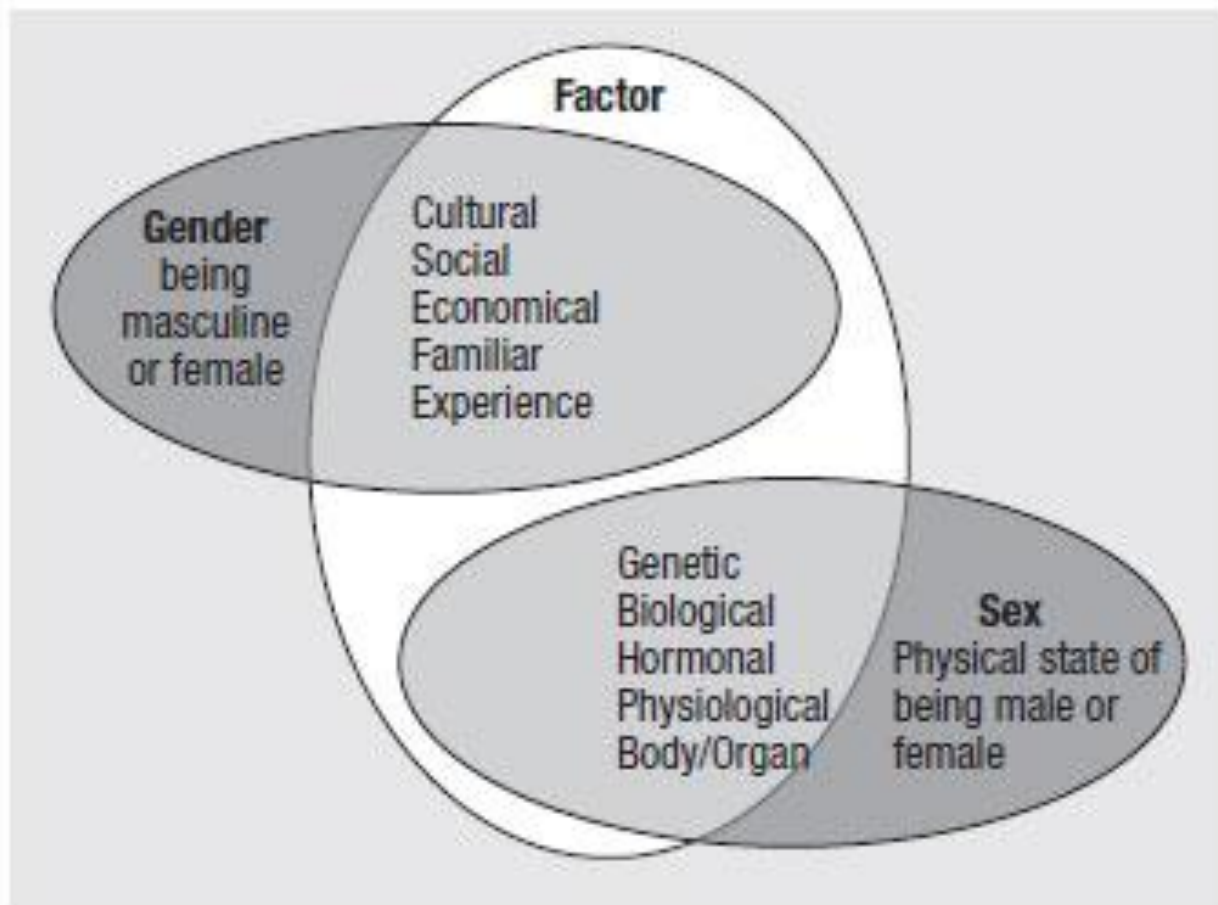


Fig. 1 | *Factors influencing gender and sex differences in human health.*

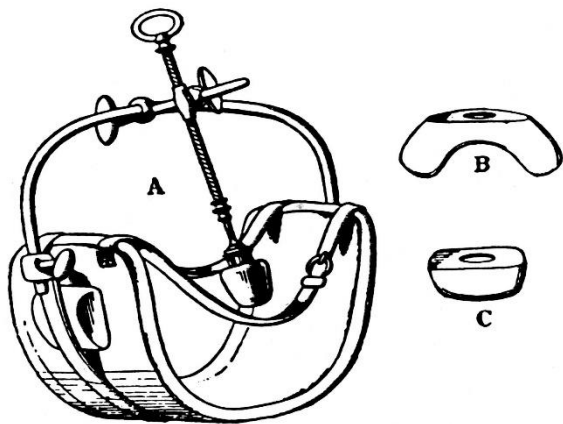
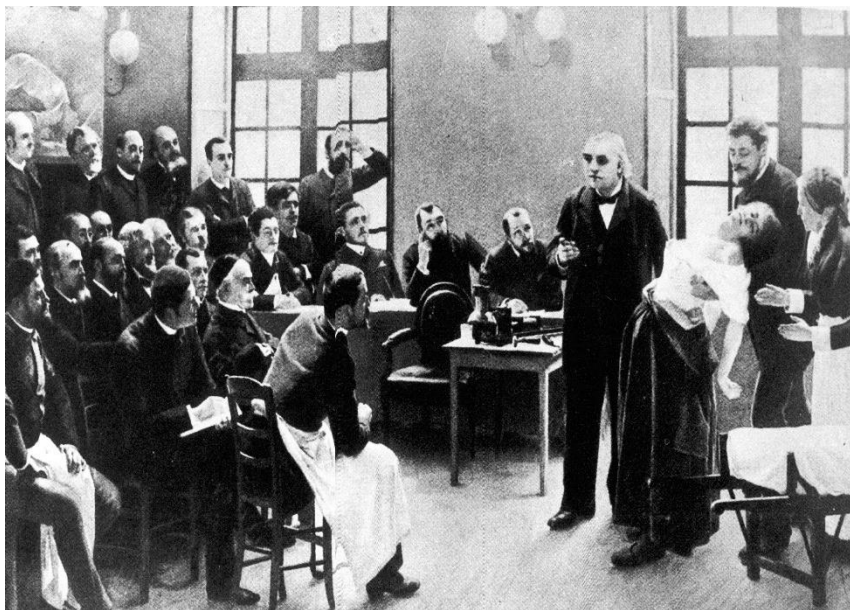
Gender-based medicine o gender medicine

è il campo della medicina che studia le differenze biologiche e fisiologiche tra i sessi umani e come queste condizionino differenze nella malattia

La **ricerca medica** è stata condotta tradizionalmente utilizzando come oggetto di studio il corpo maschile. I risultati di questi studi sono spesso stati applicati trasversalmente ad ambedue i sessi da parte dei sanitari, con un approccio indifferente nel trattamento dei maschi o delle femmine: **“cecità di genere”**

Più recentemente la ricerca medica ha cominciato a comprendere l'importanza di tenere conto del sesso in quanto i sintomi e le risposte ai trattamenti medici possono essere molto differenti tra **i due sessi** nella **prevalenza**, nella **gravità**, nella **presentazione clinica** e nella **risposta agli interventi terapeutici** di numerose malattie

La storia..



ORDINE OSPEDALIERO S. GIOVANNI DI DIO DEI FATEBENEFRAELLI
CASA DI CURA S. GIUSEPPE - VIA S. VITTORE, 12 - TELEFONI: 861.941 - 861.951
Centro Angiologico diretto dal Prof. R.

Milano, 29/5/63

Diagnostica e terapia delle malattie vascolari

Chiarissimo

ho visitato la mutuata

ed ho riscontrato eritrocianosi frigida
degli arti inferiori.

L'affezione è purtroppo resistente alle comuni
terapie.

A volte scompare definitivamente con il matrimonio.

Consiglierei la somministrazione di forti
dosi di Vitamina A ed E (Rovigon ad es.)

Localmente Delmeson schiuma.

ANGIOLOGIA
Prof.

Gender bias..



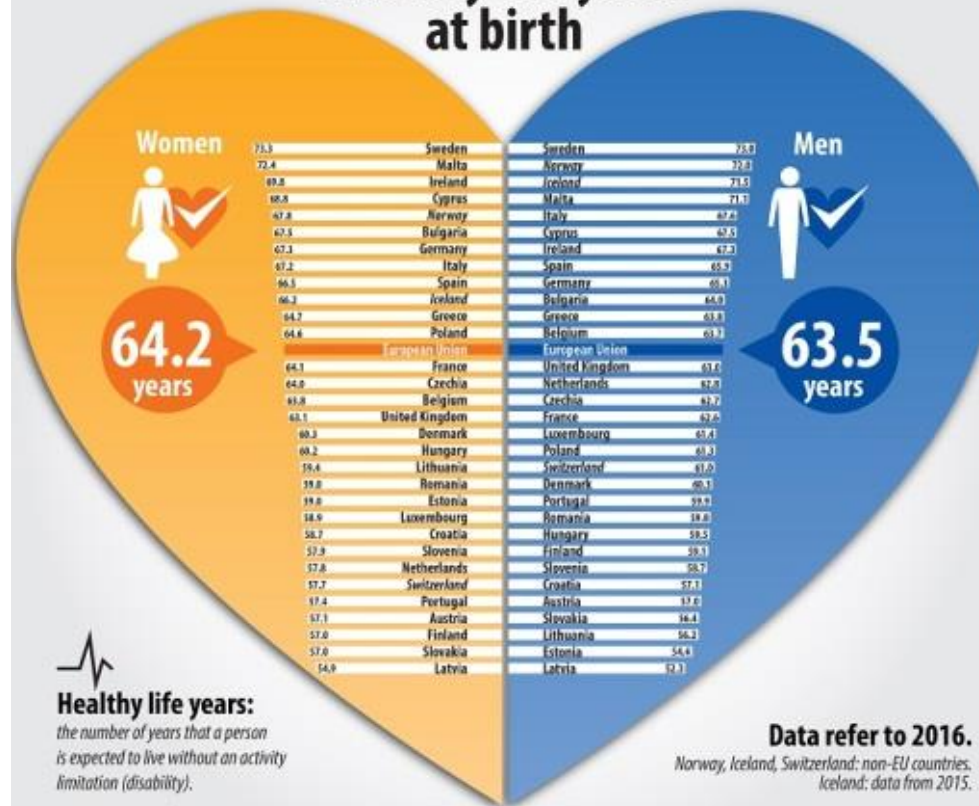
- **AUTOIMMUNITA'**
- **VARIABILITA' NELLA RISPOSTA AI FARMACI**
- **MALATTIE PSICHIATRICHE**
- **MALATTIE CARDIOVASCOLARI**
- **TROMBOEMBOLIA**

Le **donne** vivono più a lungo

La speranza di vita per loro è in media di **85,6**
anni contro i **81** degli uomini

(dato Eurostat 2016)

Healthy life years at birth



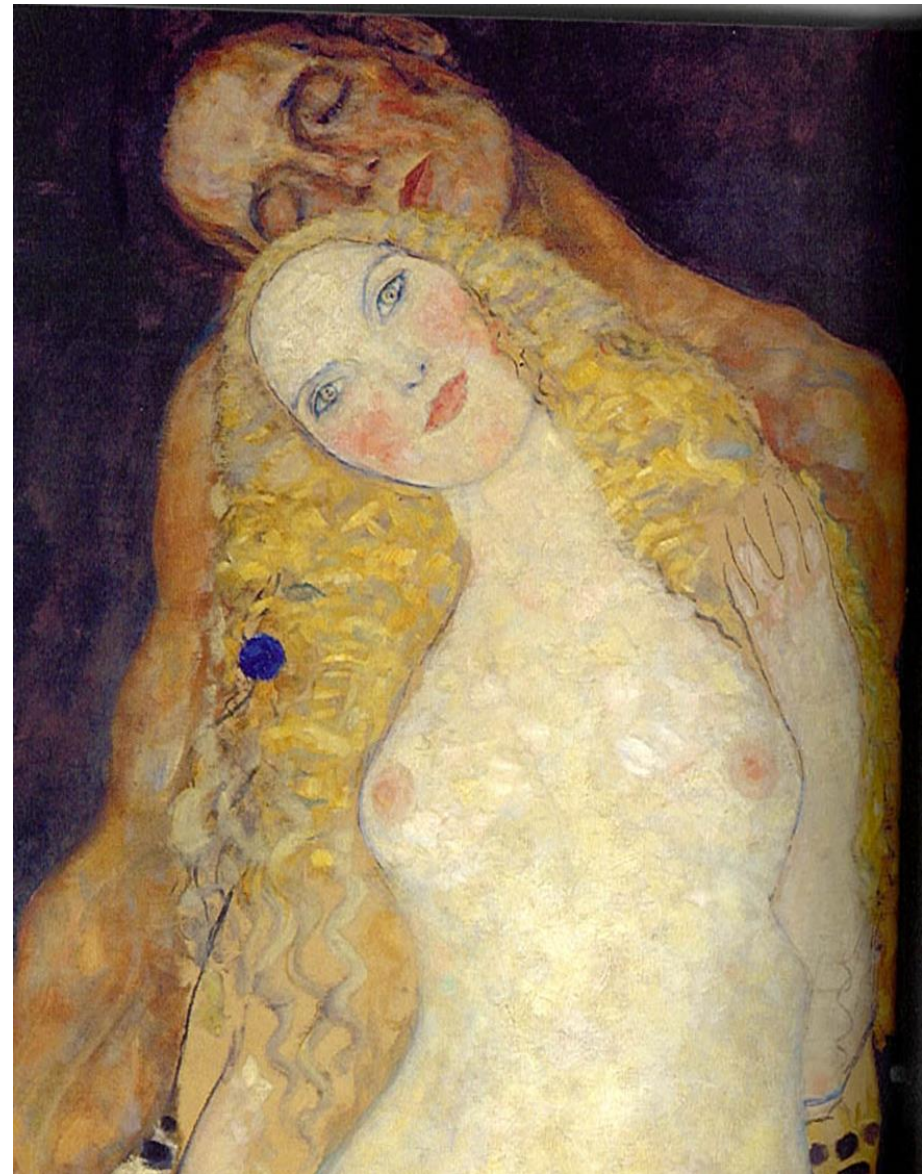
Anni di vita in buona salute (2016 e differenza 2016-2007)

Paesi	2016						Differenza 2016-2007					
	Anni di vita in buona salute in valore assoluto alla nascita - femmine	Anni di vita in buona salute alla nascita in percentuale dell'aspettativa di vita totale - femmine	Aspettativa di vita in valore assoluto alla nascita - femmine	Anni di vita in buona salute in valore assoluto alla nascita - maschi	Anni di vita in buona salute alla nascita in percentuale dell'aspettativa di vita totale - maschi	Aspettativa di vita in valore assoluto alla nascita - maschi	Anni di vita in buona salute in valore assoluto alla nascita - femmine	Anni di vita in buona salute alla nascita in percentuale dell'aspettativa di vita totale - femmine	Aspettativa di vita in valore assoluto alla nascita - femmine	Anni di vita in buona salute in valore assoluto alla nascita - maschi	Anni di vita in buona salute alla nascita in percentuale dell'aspettativa di vita totale - maschi	Aspettativa di vita in valore assoluto alla nascita - maschi
Ue 28	64,2	76,8	83,6	63,5	81,2	78,2	1,6	0,7	1,4	1,8	0,1	2,1
Belgio	63,8	76,0	84,0	63,7	80,7	79,0	-0,1	-1,4	1,4	0,2	-1,6	1,9
Bulgaria	67,5	86,0	78,5	64,0	89,8	71,3	-6,4	-10,4	1,9	-3,1	-6,7	1,8
Repubblica Ceca	64,0	78,0	82,1	62,7	82,4	76,1	0,7	-0,9	1,9	1,3	-0,8	2,3
Danimarca	60,3	72,8	82,8	60,3	76,3	79,0	-7,1	-10,8	2,2	-7,1	-12,2	2,8
Germania	67,3	80,7	83,5	65,3	83,1	78,6	8,7	9,9	0,8	6,3	6,9	1,2
Estonia	59,0	71,8	82,2	54,4	74,2	73,3	4,1	2,3	3,3	4,6	0,5	5,8
Irlanda	69,8	83,5	83,6	67,3	84,2	79,9	4,2	3,6	1,5	4,4	2,8	2,6
Grecia	64,7	77,1	84,0	63,8	80,9	78,9	-2,9	-4,8	1,5	-2,2	-4,9	2,0
Spagna	66,5	77,0	86,3	65,9	81,9	80,5	3,3	2,1	1,9	2,4	0,4	2,6
Francia	64,1	74,8	85,7	62,6	78,7	79,5	-0,3	-1,2	0,9	-0,2	-2,3	1,9
Croazia	58,7	72,2	81,3	57,1	76,1	75,0	nd	nd	2,1	nd	nd	2,8
Italia	67,2	78,5	85,6	67,6	83,4	81,0	4,6	4,2	1,4	4,2	3,0	2,2
Cipro	68,8	81,1	84,9	67,5	83,9	80,5	6,0	4,6	2,8	4,4	2,6	2,9
Lettonia	54,9	69,0	79,6	52,3	75,0	69,8	0,1	-2,9	3,4	0,9	-3,8	4,5
Lituania	59,4	74,2	80,1	56,2	80,9	69,5	1,3	-1,1	2,9	2,9	-1,7	5,0
Lussemburgo	58,9	69,0	85,4	61,4	76,7	80,1	-5,7	-9,6	3,2	-0,9	-4,5	3,4
Ungheria	60,2	75,5	79,7	59,5	82,0	72,6	2,4	1,2	1,9	4,4	2,6	3,2
Malta	72,4	85,8	84,4	71,1	88,2	80,6	1,3	-0,7	2,2	1,9	-1,1	3,1
Paesi Bassi	57,8	69,5	83,2	62,8	78,5	80,0	-6,5	-8,4	0,7	-3,3	-6,1	1,9
Austria	57,1	67,9	84,1	57,0	71,9	79,3	-4,3	-6,0	1,0	-1,7	-4,0	1,9
Polonia	64,6	78,8	82,0	61,3	82,9	73,9	3,1	1,7	2,2	3,7	1,8	2,9
Portogallo	57,4	68,1	84,3	59,9	76,7	78,1	-0,5	-2,0	1,8	1,4	-0,4	2,2
Romania	59,0	74,6	79,1	59,8	83,4	71,7	-3,5	-6,8	2,3	-0,7	-3,6	2,2
Slovenia	57,9	68,7	84,3	58,7	75,0	78,2	-4,4	-7,3	2,3	0,0	-3,7	3,6
Slovacchia	57,0	70,6	80,7	56,4	76,4	73,8	0,9	-0,9	2,3	0,8	-2,3	3,2
Finlandia	57,0	67,6	84,4	59,1	75,2	78,6	-1,0	-2,2	1,3	2,3	0,4	2,6
Svezia	73,3	87,2	84,1	73,0	90,6	80,6	6,5	6,8	1,0	5,3	4,9	1,6
Regno Unito	63,1	76,0	83,0	63,0	79,4	79,4	-2,9	-4,7	1,2	-1,6	-3,8	1,8

Fonte: elaborazione su dati Eurostat

sesto, genere e salute: un nuovo approccio

- Il sesso gioca una parte importante nella salute e nella malattia
- Una ricerca multidisciplinare è la chiave per comprendere le differenze di genere
- La ricerca di base e clinica indirizzata ad espandere le conoscenze sui determinanti di queste differenze (sesso/genere, immunità, risposta ai farmaci, diversa longevità) faciliterà lo sviluppo di strategie mirate per la prevenzione, la diagnosi e la terapia delle malattie





Azienda Ospedaliera
Ospedale Niguarda Ca' Granda

Convegno

SCLEROSI MULTIPLA E DONNA

Milano

15 Maggio 2003

con il patrocinio di:



Regione Lombardia
Sanità

Aula Magna

Azienda Ospedaliera
Ospedale Niguarda Ca' Granda
Piazza Ospedale Maggiore, 3 – 20162 Milano

Neurol Sci (2004) 25:S627–S630

SIMPOSIO: DONNA E MALATTIE NEUROLOGICHE

A. Protti

La malattia neurologica nella donna: attualità e prospettive

Indagine Conoscitiva

GRUPPO DI STUDIO **DONNA E MALATTIE NEUROLOGICHE**

INDAGINE CONOSCITIVA

1) Nella tua pratica clinica consideri rilevanti i concetti di sesso e genere nella pianificazione degli interventi diagnostici e terapeutici?

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.....
.....

2) Ritieni che vi sia un sufficiente retroterra culturale e organizzativo per affrontare le problematiche connesse a sesso e genere nella pratica clinica?

.....
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.....

3) Ritieni necessaria la produzione/implementazione di protocolli/linee guida per la gestione delle patologie neurologiche nella donna?

.....
.....
.....

4) Ritieni che il neurologo sia sufficientemente preparato per fornire indicazioni inerenti la contraccezione, la gravidanza, il parto, la menopausa?

.....
.....
.....

5) Proponi un percorso clinico per la gestione della contraccezione orale nelle donne con emicrania - pregressi eventi trombotici - familiarità per trombosi?

.....
.....

6) Ritieni sufficiente la preparazione del neurologo sul rischio teratogeno dei farmaci?

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.....
.....

7) Ritieni che il genere abbia una rilevanza nella comunicazione interpersonale in campo sanitario?

.....
.....
.....

8) Ritieni importante la valutazione della variabilità correlata al genere nella risposta ai farmaci?

.....
.....
.....
.....

9) Ritieni che vi sia un pregiudizio di genere nell' approccio alla sperimentazione clinica?

.....
.....
.....

10) Ritieni che vi sia una differenza di accesso alle cure e di diritto alla salute correlate al genere?

.....
.....
.....

11) Ritieni che vi siano specificità di genere in campo bioetico?

.....

12) Ritieni utile la terapia sostitutiva ormonale in donne in menopausa per la prevenzione della demenza e/o delle malattie cerebrovascolari?

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13) Quali sono le problematiche cliniche ed organizzative che individui come prioritarie nel lavoro del gruppo di studio?

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Facoltativo:

NOME e COGNOME.....

POSIZIONE.....

PROFESSIONALE.....

INDIRIZZO.....

PROFESSIONALE.....

TEL FAX..... CELL.....

E-mail.....

Tutela della privacy/Trattamento dei dati personali: i suoi dati personali saranno trattati nel rispetto della legge 675/96, che lei con la firma della presente scheda autorizza. In qualsiasi momento, ai sensi dell'articolo 13 di detta legge, potrà consultare, modificare o far cancellare i Suoi dati od opporsi al loro utilizzo.

Firma.....



13) Quali sono le problematiche cliniche ed organizzative che individui come prioritarie nel lavoro del gruppo di studio?

- ***Produzione/implementazione protocolli e linee guida***
- ***Problematiche neurologiche correlate alla gravidanza, contraccezione e menopausa***
- ***Problematiche della gravidanza (trattare, non trattare, timing, dosaggi, ecc)***
- ***Studi mirati a valutazione rischio/beneficio di terapie ormonali sostitutive***
- ***Suddivisione in gruppi di lavoro per tematiche***
- ***Creazione di una rete nazionale per condivisione di casistiche e gestione di casi clinici complessi***

Woman's Health



Sclerosi Multipla
banco di prova della medicina di genere

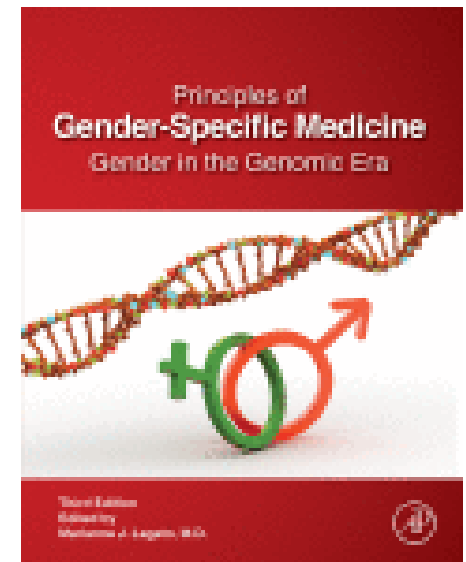
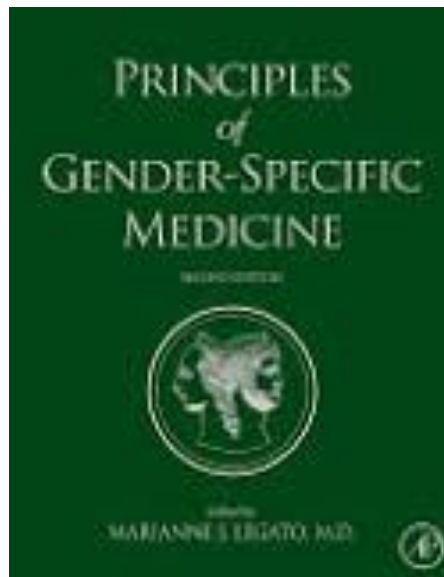
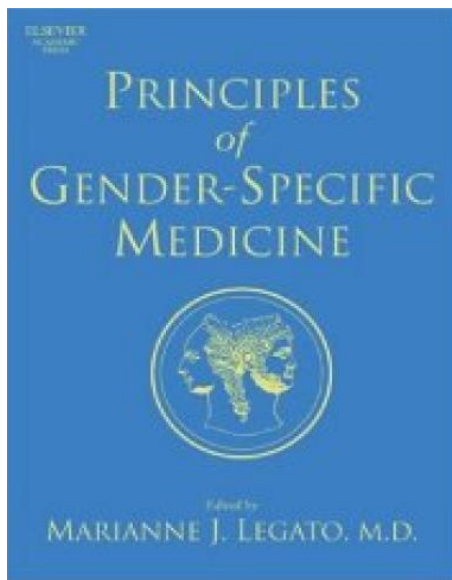
Table 1 Publications with sex and gender differences in the most frequent clinical entities

Cardiology	Rheumatology/ immunology	Pneumology	Nephrology	Gastroenterology/ hepatology	Neurology	Endocrinology	Oncology	Hematology
Hypertension (414)	Lupus erythematosus (68)	Asthma (140)	Renal failure (27)	Hepatitis B (22)	Multiple sclerosis (65)	Diabetes mellitus (447)	Skin carcinoma (45)	Anemia (44)
Myocardial infarction (275)	Rheumatoid arthritis (41)	Lung cancer (116)	Diabetic nephropathy (11)	Hepatitis C (26)	Stroke (129)	Obesity (349)	Gastric cancer (25)	Leukemia (49)
Heart failure (153)	Systemic sclerosis (3)	Chronic obstructive pulmonary disease (36)	Glomerulone phritis (9)	Hepatocellular carcinoma (37)	Alzheimer's disease (104)	Osteoporosis (123)	Renal cell carcinoma (17)	Lymphoma (34)
Atrial fibrillation (38)	Fibromyalgia (15)	Pulmonary hypertension (12)	Polycystic kidney disease (12)	Inflammatory bowel disease (13)	Epilepsy (56)	Hypothyroidism (33)	Bladder cancer (22)	Thrombocytopenia (6)
Coronary heart disease (207)	Sjögren's syndrome (8)	Pulmonary embolism (11)	Renal artery stenosis (0)	Colorectal cancer (24)	Parkinson's disease (69)	Hyperthyroidism (16)	Thyroid carcinoma (16)	Purpura (2)
Cardiomyopathy (41)	Ankylosing spondylitis (11)	Sarcoidosis (6)	IgA nephropathy (2)	Autoimmune hepatitis (2)	Muscular dystrophy (11)	Morbus addison/ Cushing's disease (5)	Pancreatic carcinoma (10)	Agranulocytosis (0)

Numbers of relevant publications are in brackets

Vera Regitz-Zagrosek

EMBO reports VOL 13 | NO 7 | 2012



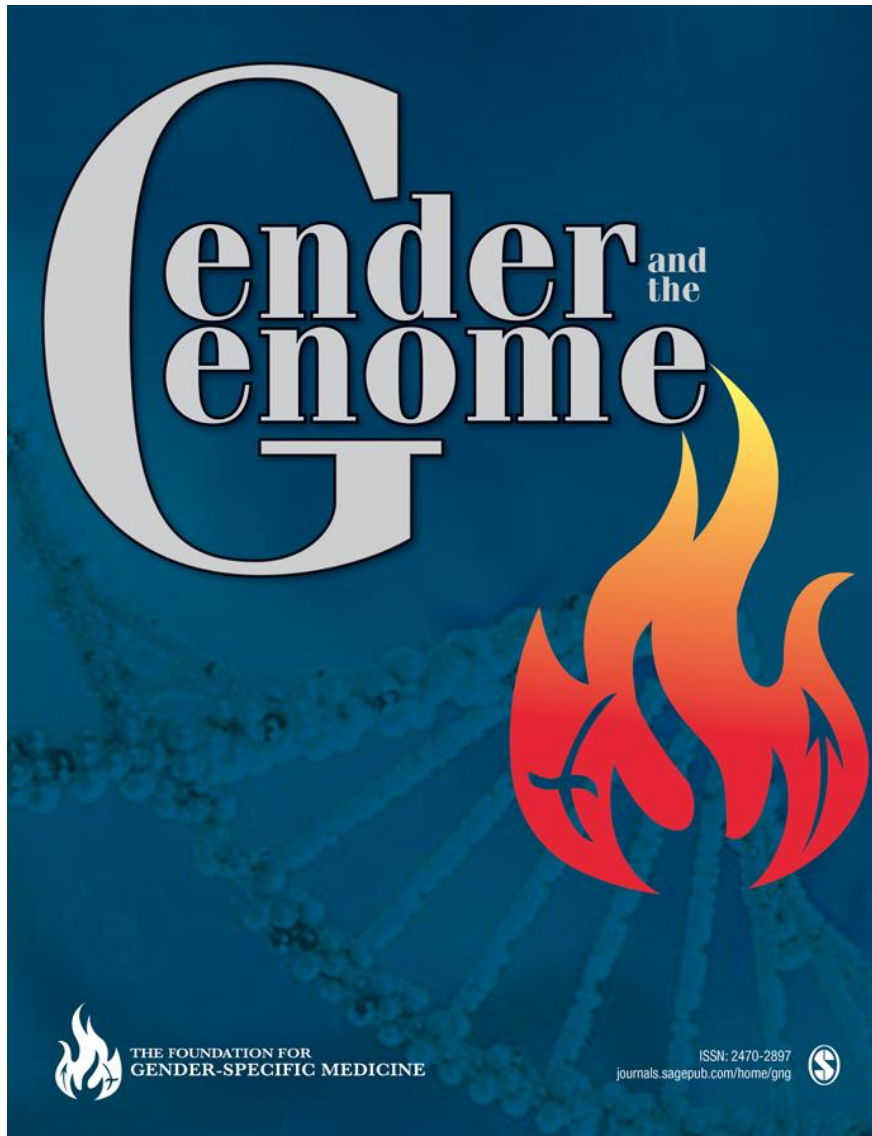
«I maschi e le femmine hanno una diversa attesa di vita, sviluppano malattie differenti e spesso presentano un diverso decorso della medesima condizione morbosa

comprendere la base di queste differenze di sesso
è importante per sviluppare nuove strategie di prevenzione, diagnosi e terapia

con la possibilità di un beneficio per la donna, ma anche per l'uomo»

Ed: Marianne J. Legato
"Principles of Gender-Specific Medicine"
2 vol, Elsevier Acad Press, 2004
2008
2017

L'ultima edizione enfatizza le conoscenze sulla biologia molecolare e le scienze genomiche in una varietà di discipline..



Gender and the Genome is a peer reviewed, open access journal that provides evidence-based original research, reviews, perspectives, and commentaries that illuminate the impact of biological sex on technology and its effects on human life. The journal is the official journal of [the Foundation for Gender-Specific Medicine](#), [the International Society for Gender-Specific Medicine](#), and [the Israeli Society for Gender-and Sex Conscious Medicine](#).

Sex Differences Research, Precision Medicine, and the Future of Women's Health

Virginia M. Miller, PhD,¹ Walter A. Rocca, MD, MPH,² and Stephanie S. Faubion, MD³

Patient-centered, precision medicine defines 21st century health care. Viewing the patient through a sex and gender lens is a first step toward personalizing care. However, personalized healthcare must be based on evidence derived from research designed to study how sex and hormonal status influence health across the life-span. The Mayo Clinic approach to translation of women's health research into clinical practice is embodied by innovative technologies driving discovery in regenerative medicine, organ and tissue transplantation, and pharmacogenomics. This approach may serve as a model by which other academic institutions can expand their women's health research programs. Ongoing initiatives in healthcare education are required to assure that future healthcare providers, researchers, and educators recognize that sex matters when making decisions about prevention, diagnosis, disease management, and patient outcomes. A plan to successfully integrate sex difference research and precision medicine should include research of sex-specific conditions.



Presidenza del Consiglio dei Ministri

COMITATO NAZIONALE PER LA BIOETICA

LA SPERIMENTAZIONE FARMACOLOGICA SULLE DONNE

(28 novembre 2008)

- Sottorappresentatività nell' arruolamento delle donne e carenze nell'analisi differenziata dei dati
- I cambiamenti della salute/malattia nelle donne
- Le donne consumatrici di farmaci e il problema degli effetti collaterali
- La donna come "soggetto debole"
- L' esclusione/inclusione delle donne in età fertile nei protocolli di sperimentazione
- Presenza di donne nelle equipe mediche e nei comitati etici
- Linee guida bioetiche internazionali
- La normativa nazionale
- Raccomandazioni bioetiche

Vera Regitz-Zagrosek *Editor*

Sex and Gender Differences in Pharmacology

 Springer

5 Conclusion

Because of the prominent role of gender, it seems mandatory to construct individualized clinical care algorithms based on individual risk profiles on top of gender-based assessment.

Take Home Messages

- Sex and gender differences in frequent diseases—such as cardiovascular diseases, pulmonary diseases, gastroenterology and hepatology, in nephrology, autoimmune diseases, endocrinology, hematology, neurology—are widespread.
- Sex and gender differences have significant consequences on the daily practice of medicine, on outcomes and effects of therapies.
- Gender medicine is a novel medical discipline that takes into account the effects of sex and gender on the health of women and men. The major goal is to improve health and health care for both, for women as well as for men.
- Drug development is still preferentially based on male animals and women are underrepresented in early and cardiovascular clinical trials.
- Management and drug use differs in women and men.
- Most guidelines do not include even well-known sex and gender differences. European guidelines for the management of cardiovascular diseases in pregnancy have only recently been published.
- Personalized medicine cannot replace gender-based medicine. The sociocultural dimension of gender integrating lifestyle, environment, stress, and other variables cannot be replaced by a sum of biological parameters.

Themed Section: Biological Sex and Cardiovascular Pharmacology

REVIEW

Pharmacogenomics, pharmacokinetics and pharmacodynamics: interaction with biological differences between men and women

Flavia Franconi^{1,2} and Ilaria Campesi^{2,3}

Correspondence

Professor Flavia Franconi,
Department of Biomedical
Sciences, University of Sassari,
Via Muroni 23, 07100 Sassari,
Italy. E-mail: franconi@uniss.it

Keywords

sex differences; gender
differences; drug response;
pharmacodynamics;
pharmacokinetic

Received

13 February 2013

Revised

5 August 2013

Accepted

16 August 2013

CSD Grand Rounds**Gaps in Knowledge in Treating Pregnant Women****Donald Mattison, MD, and Anne Zajicek, MD, PharmD**

Table III. Sex differences in the experience of adverse events.

Possible Clinical Factor	Pharmacologic Factor	Physiological and Molecular Factors
Women are overdosed	Pharmacokinetic	Volume of distribution is smaller Free fraction of drug is larger Clearance from the body is slower
Women take more medications	Drug interaction	Alteration in pharmacokinetics (see above) Alteration in pharmacodynamics (see below)
Women are more sensitive	Pharmacodynamic	Alteration in receptor number Alteration in receptor binding Alteration in signal transduction pathway after receptor binding



Gender differences in adverse drug reactions reported to the national pharmacovigilance centre in the Netherlands An explorative observational study.

de Vries ST¹, Denig P¹, Ekhart C², Burgers JS^{3,4}, Kleefstra N^{5,6,7}, Mol PGM^{1,8}, van Puijenbroek EP^{2,9}.

Quaderni
del Ministero
della Salute

ISSN 2038-5293

26

n. 26, aprile 2016

Il genere come determinante di salute

Lo sviluppo della medicina di genere per garantire
equità e appropriatezza della cura





Verso una Medicina Genere – Specifica



21 e 22 marzo 2017
Istituto Superiore di Sanità
Aula Pocchiari
Viale Regina Elena, 299
ROMA

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THE ITALIAN JOURNAL of Gender-Specific MEDICINE

Volume 4, Issue 2 — 2018

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in clinical research and health
policy implications
ARIANDO PERES

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pharmacology of statins: an update
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53 Provocative testing in women
with suspected ischemic heart
disease: an insight into daily
clinical practice
DAVIDE ERMACORA, RENATO RAZZOLINI

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between energy metabolism and
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in the Lombardy Region
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in reumatologia e il punto di vista
della SIR

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SocioSanitaria Rhodense nell'ambito
della medicina di genere specifica

85 Sclerosi multipla: un progetto
di Onda per conoscerla
e raccontarla, guardando al futuro

87 Donne e migrazioni: la triplice
invisibilità





European Charcot Foundation
Co-ordination of Multiple Sclerosis Research in Europe

**EUROPEAN CHARCOT FOUNDATION
SYMPOSIUM 2008**

MULTIPLE SCLEROSIS AND GENDER

November 13-15, 2008

Complessità nella donna

**Variazioni ormonali
correlate a fasi della vita
femminile:**

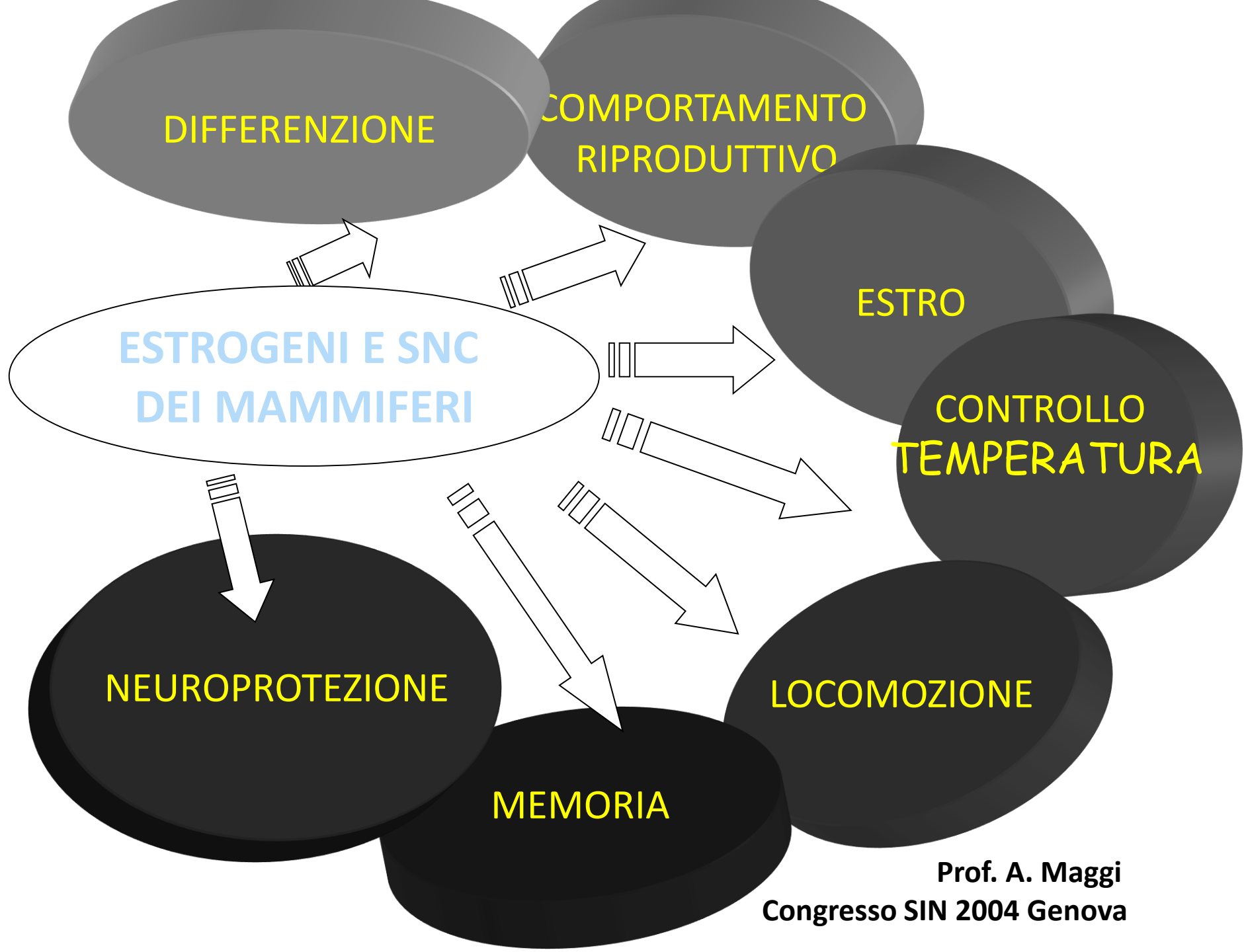
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ciclo mestruale gravidanza

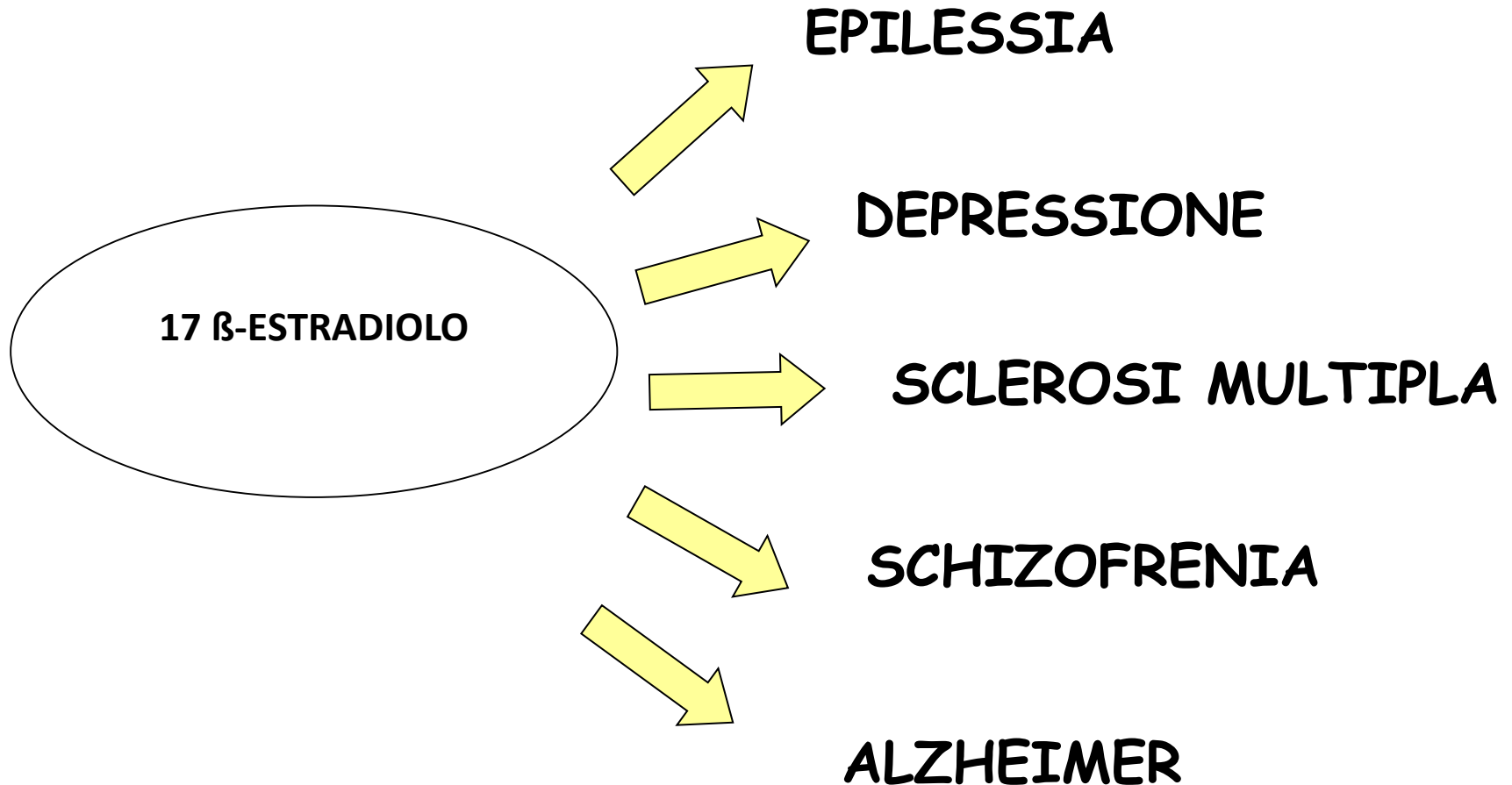
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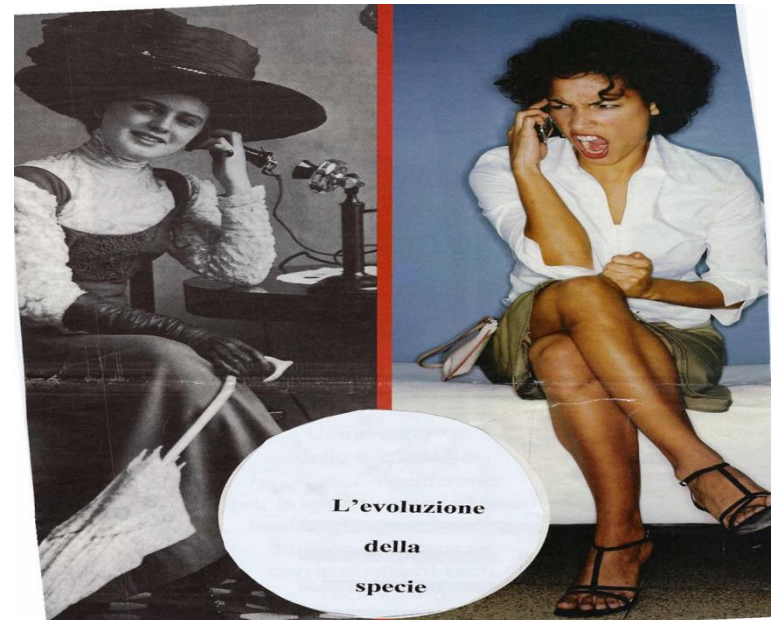
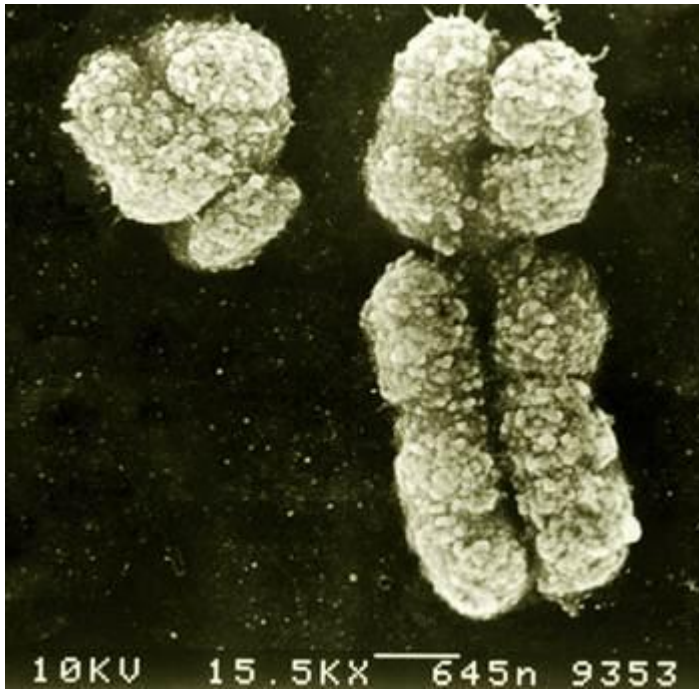


ESTROGENI E PATOLOGIE DEL SNC



SESSO

Prof. A. Piazza
Congresso SIN Bari 2006



GENERE



mmine costituiscono un
ico naturale (Mary Lyon):
vazione del cromosoma X

single cell

dy exert widespread and sometimes unexpected effects.

help to explain why women and men
rent susceptibilities to conditions
esity, heart disease, neurodegenera-
community and cancer, and why such

understanding sex differences in disease. "In
disease, one of the sex-biasing factors may be
suppressed, leaving the others to have a big-
ger effect," explains Art Arnold, a biologist at

ZARA PICKEN

Learning from Nature: Pregnancy Changes the Expression of Inflammation-Related Genes in Patients with Multiple Sclerosis

Francesca Gilli^{1*}, Raija L. P. Lindberg², Paola Valentino¹, Fabiana Marnetto¹, Simona Malucchi¹, Arianna Sala¹, Marco Capobianco¹, Alessia di Sapio¹, Francesca Sperli¹, Ludwig Kappos², Raffaele A. Calogero³, Antonio Bertolotto¹



Contents lists available at [SciVerse ScienceDirect](#)

Journal of Autoimmunity

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



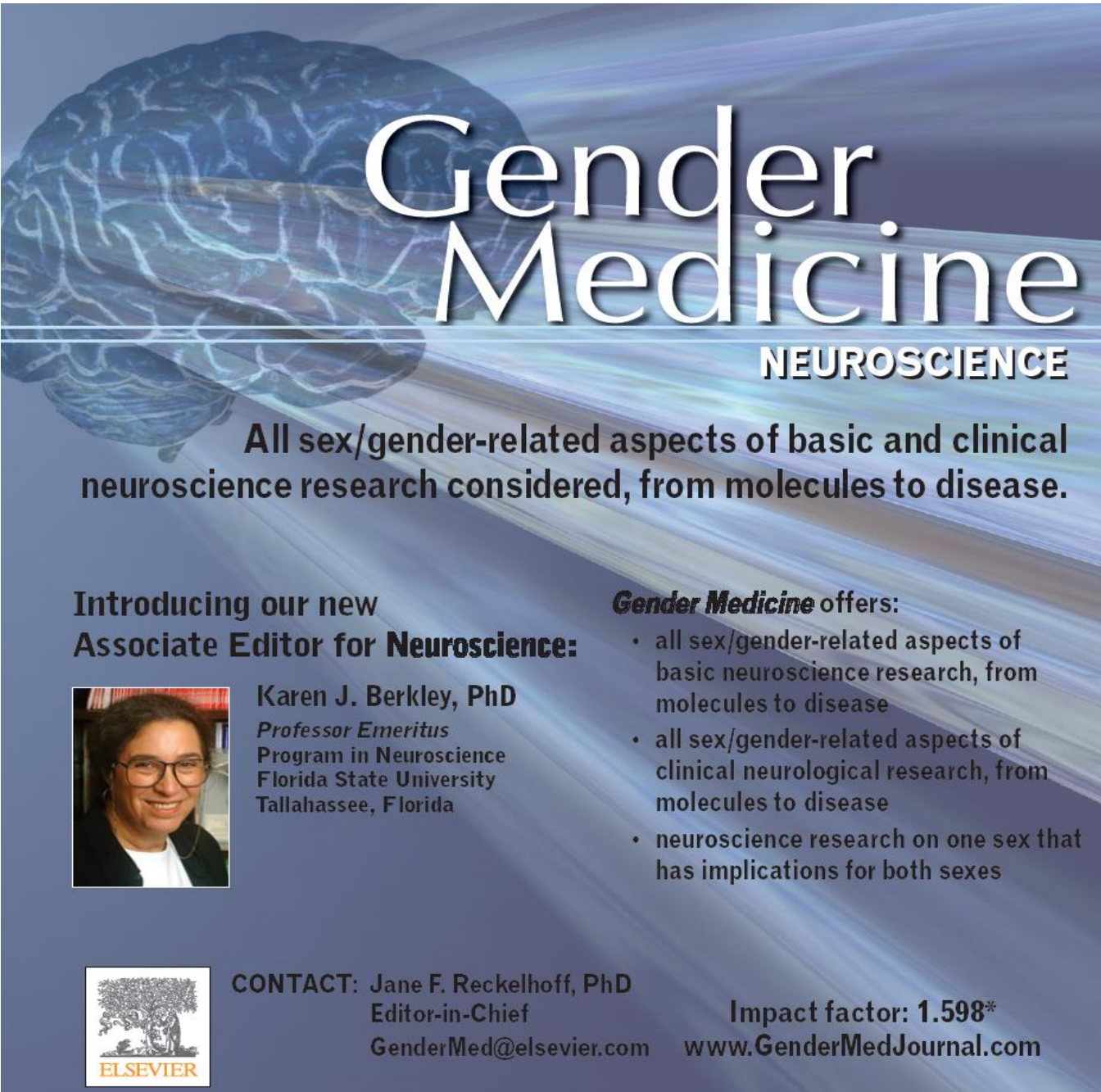
Gender-based blood transcriptomes and interactomes in multiple sclerosis: Involvement of SP1 dependent gene transcription

Ramesh Menon^{a,b,1}, Marco Di Dario^{a,b,1}, Chiara Cordiglieri^{a,b}, Silvia Musio^b, Loredana La Mantia^b,
Clara Milanese^b, Anna Luisa Di Stefano^c, Massimo Crabbio^c, Diego Franciotta^d, Roberto Bergamaschi^c,
Rosetta Pedotti^b, Enzo Medico^e, Cinthia Farina^{a,b,*}

^a Institute of Experimental Neurology (INSpe), Division of Neuroscience, San Raffaele Scientific Institute, Milan, Italy

^b Neuroimmunology and Neuromuscular Disorders Unit, Foundation IRCCS Neurological Institute Carlo Besta, Milan, Italy

^c Department of Biomedical Sciences, Foundation IRCCS Neurological Institute Carlo Besta, Milan, Italy



Gender Medicine

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CONTACT: Jane F. Reckelhoff, PhD
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GenderMed@elsevier.com

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Sono state costituite la

- **Società Italiana per la Salute e la Medicina di Genere**
- **Società Europea per la Salute e la Medicina di Genere**



**Presentazione ai neurologi
nell'ambito del
Congresso SIN 2008 Napoli**

Donna e Sclerosi Multipla

VICENZA



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SEDE

venedì

14.00 - 14.30

9 giugno 2006

Registrazione Partecipanti

Welcome coffee

14.30 - 14.45

Benvenuto e introduzione

Moderatori: C. Milanese - R. Capra

14.45 - 15.15

Peculiarità della SM nella donna

A. Protti

15.15 - 15.50

SM, sistema immunitario e ormonale: differenze di genere

P. Gallo

15.50 - 16.15

Coffee Break

16.15 - 16.45

SM aspetti genetici

S. Penco

16.45

Discussione

Tutti i relatori e moderatori

sabato

8.30 - 8.45

Registrazione Partecipanti

8.45 - 9.00

Introduzione

Moderatori: A. Protti - G. Mosetta

9.00 - 9.30

SM, catamenialità e contraccezione

M. Bortolan

9.30 - 10.00

SM e fertilità

M. Bini

10.00 - 10.30

SM gravidanza e parto

F. Bortolan

10.30 - 10.50

Discussione

Tutti i relatori e moderatori

10.50 - 11.10

Coffee Break

11.10 - 11.15

Ripresa dei lavori

Moderatori: M. Zaffaroni - M. Zoczon

11.15 - 11.45

SM, puerperio e allattamento

A. Ghiszi - M. Zaffaroni

11.45 - 12.15

I rischi da farmaci nella donna con SM

R. Leone

12.15 - 12.45

Discussione

Tutti i relatori e moderatori

12.45 - 14.25

Pranzo

14.25 - 14.30

Ripresa dei lavori

Moderatori: F. Bortolan - A. Ghiszi

14.30 - 15.00

SM e sessualità

M. Zoczon

15.00 - 15.40

Problematiche psicosociali ed economiche nella donna con SM

C. Zuliani - L. Decio

15.40 - 16.00

Conclusioni e chiusura dei lavori

F. Bortolan - A. Protti - M. Bortolan

16.00 - 16.30

Compilazione questionario ECM

Emicrania e differenze di genere

Relatori e Moderatori del I Modulo

Elio Agostoni
SC Neurologia e Stroke Unit, Lecco e Merate, Dipartimento di Neuroscienze
AO Ospedale di Lecco

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Dipartimento di Neuroscienze Cliniche Ospedale S Giacomo, Novi Ligure (AL)
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Le differenze di genere e la neurologia

Corso in 6 moduli
Lecco, novembre 2008-giugno 2009

Emicrania
Sclerosi Multipla
Malattia di Parkinson
Epilessia
Stroke
Urgenze neurologiche in gravidanza

Presidente del corso

Elio Agostoni

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Manuela Vaccaro



CORSO
le differenze di genere
e la neurologia

Lecco, novembre 2008 - giugno 2009



Emicrania e
differenze di genere

I modulo 12 Novembre 2008

Sin Gruppo di studio Donna
e Malattie Neurologiche





III modulo
**MALATTIA DI PARKINSON,
DISTURBI DEL MOVIMENTO E
DIFFERENZE DI GENERE**
22 aprile 2009

IV modulo
**EPILESSIA E
DIFFERENZE DI GENERE**
5 novembre 2009

V modulo
**MALATTIA CEREBROVASCOLARE E
DIFFERENZE DI GENERE**
18 novembre 2009



Padova: 8 marzo 2011



NEUROLOGIA AL FEMMINILE: *essere donna nella patologia neurologica*

CON L'ALTO PATROCINIO DEL
PRESIDENTE DELLA REPUBBLICA

*Dopo aver riflettuto bene sul
destino delle donne in tutti i
tempi e in tutti i paesi, ho finito
per convincermi che ogni uomo
dovrebbe dire a ogni donna
invece del buongiorno:
"Perdonateci"!" perchè i più
forti hanno fatto la legge".*

Alfred de Vigny, diario di un poeta, 1867 (postumo)

Dedicato a

Elena Lucrezia Cornaro
Piscopia

prima donna laureata e a
tutte le donne del mondo





Nuove frontiere in Medicina: la Medicina di Genere

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9.00 Saluto delle Autorità:

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Presidente Centro Studi Nazionale su Salute e Medicina di Genere - G. Baggio
Presidente GIGeG - Gruppo Italiano Salute e Genere - F. Francini

9.30 Il Comitato Unico di Garanzia ed il progetto Women Friendship e Medicina di Genere

M. Coen
Presidente CUG
AOU S. Giovanni Battista di Torino
A. Ianni Palarchio
Università degli Studi di Torino

I SESSIONE

Moderatori: M.T. Giordana, C. Bucca, P. Crosasso

10.00 Lettura Magistrale: Neurologia di Genere

A. Protti - A.O. Ospedale Niguarda Cà Granda - Milano

10.30 La sclerosi multipla

P. Cavalla - AOUS. Giovanni Battista di Torino

10.50 Il sonno e le donne

A. Cicolin - Università degli Studi di Torino

11.15 Pausa Caffè

11.30 Lettura Magistrale: Malattie metaboliche dell'osso

G. Isala - Università degli Studi di Torino

12.00 L'osteoporosi e la rimborsabilità dei farmaci

M. Procopio - AOUS. Giovanni Battista di Torino

12.20 La vescica iperattiva

R. Carone, A. Biroti - AO CTO-Maria Adelaide di Torino
Osp. S. Giovanni Bosco di Torino

12.40 Discussione

13.15 Pausa pranzo

II SESSIONE

Moderatori: T. Cammarota, P. Omedè, M.T. Sorrentino

14.00 Lettura Magistrale: Trials clinici e melanoma in fase avanzata

M.G. Bemengo - Università degli Studi di Torino

14.30 Esiste un Bias di Genere nella Sperimentazione Clinica in Oncologia?

A. Ianni Palarchio - Università degli Studi di Torino

14.50 Psoriasi: terapia di genere

A. Parodi - Università degli Studi di Genova

15.10 La prevenzione della malattia cardiovascolare nella donna

C. Grasso - AOUS. Giovanni Battista di Torino

15.30 La donna e l'alcool

V. Gallo - Università degli Studi di Torino

15.50 La percezione del dolore nei due generi

A. De Luca - AOUS. Giovanni Battista di Torino

16.10 Discussione finale

16.30 Considerazioni conclusive

17.00 Test ECM



Differenze di genere nelle patologie cardiologiche e neurologiche

MILANO, 05 MARZO 2010
Sala Multimediale - Sede ISPESL
Via L. Mangiagalli, 3

Con il patrocinio di:



Provincia di Milano

Gruppo Studio
Donna e Malattie
Neurologiche
della SIN

III° Convegno sulla Medicina di Genere



La Sclerosi Multipla: una malattia al femminile

06 Marzo 2012
Sala Auditorium Politecnico
Via Giovanni Pascoli 53, Milano

Promosso da:
Comitato Unico di Garanzia per le Pari Opportunità,
la valorizzazione del benessere di chi lavora
e contro le discriminazioni (C.U.G.)
Fondazione IRCCS Istituto Neurologico Carlo Besta

Con il patrocinio di:



Gruppo Studio
Donna e Malattie
Neurologiche
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TUTTA CUORE E CERVELLO

II° Convegno sulla Medicina di Genere



Milano, 04 marzo 2011
Sala Multimediale - Sede ISPESL - Via L. Mangiagalli, 3

Promosso da:
Comitato per le Pari Opportunità
Fondazione IRCCS Istituto Neurologico Carlo Besta

CURARE, CURARSI, PRENDERSI CURA:
LA MALATTIA DI ALZHEIMER E LE MALATTIE RARE

WSA

WOMEN STROKE ASSOCIATION

2-3 Dicembre 2011

WSA CONFERENCE: HEART AND BRAIN DISEASES IN WOMEN

www.womenstrokeassociation.org



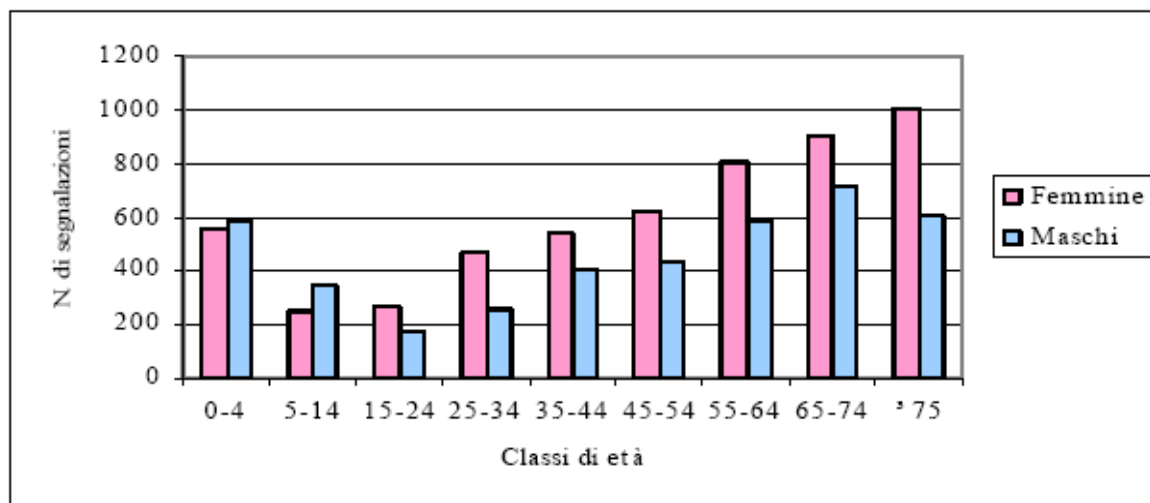
2010

Prof. Flavia Franconi
Farmacologia Cellulare Università di Sassari
Gruppo Italiano Salute e Genere

sito www.giseg.org

Congresso SIN 2006 Bari

Adrs per sesso ed età



Fonte dei dati e anno di riferimento: Elaborazione AIFA dalla Rete Nazionale di Farmacovigilanza. Anno 2007

Osservatorio AIFA

Area terapeutica	SC donne	%	% Italia
Oncologia	258	62,6	28,1
Ginecologia e ostetricia	73	17,7	1,7
Malattie apparato muscolo-scheletrico	33	8,0	2,7
Endocrinologia	11	2,7	5,8
Neurologia	7	1,7	8,2
Sistema genito-urinario	6	1,5	1,6
Anestesiologia	6	1,5	1,4
Immunologia e malattie infettive	5	1,2	9,4
Nefrologia/Urologia	5	1,2	3,4
Dermatologia/Chirurgia plastica	4	1,0	2,2
Cardiologia/Malattie vascolari	1	0,0	11,1
Gastroenterologia	1	0,0	7,0
Psichiatria/Psicologia	1	0,0	2,8
Farmacologia/Tossicologia	1	0,0	0,8
Totale	412	100,0	100,0

Sperimentazioni cliniche su donne per area terapeutica (dati AIFA 01/01/2000 - 31/12/2006)

Classe terapeutica	Sperimentazioni cliniche controllate	N. soggetti	Donne (%)
Trombolitici	176	279.179	24.1
Antitrombotici	103	167.878	27.0
Antiarritmici	80	45.430	22.6
Beta bloccanti	70	56.517	20.6
Antiaggreganti	69	91.172	24.0

Nature/ vol465/ 10 June 2010

www.nature.com/nature

Putting gender on the agenda

Editoriale pag 665

Sex bias in trials and treatment must end

Alison M. Kim, Candace M. Tingen, Teresa K. Woodruff

Pag 688-689

Male still dominate animal studies

Irving Zucker, Annalise K. Beery

Pag 690

CORRESPONDENCE

Open Access

Analysis of sex and gender-specific research reveals a common increase in publications and marked differences between disciplines

Sabine Oertelt-Prigione^{1*}, Roza Parol^{1,2}, Stephan Krohn¹, Robert Preißner², Vera Regitz-Zagrosek^{1,3}

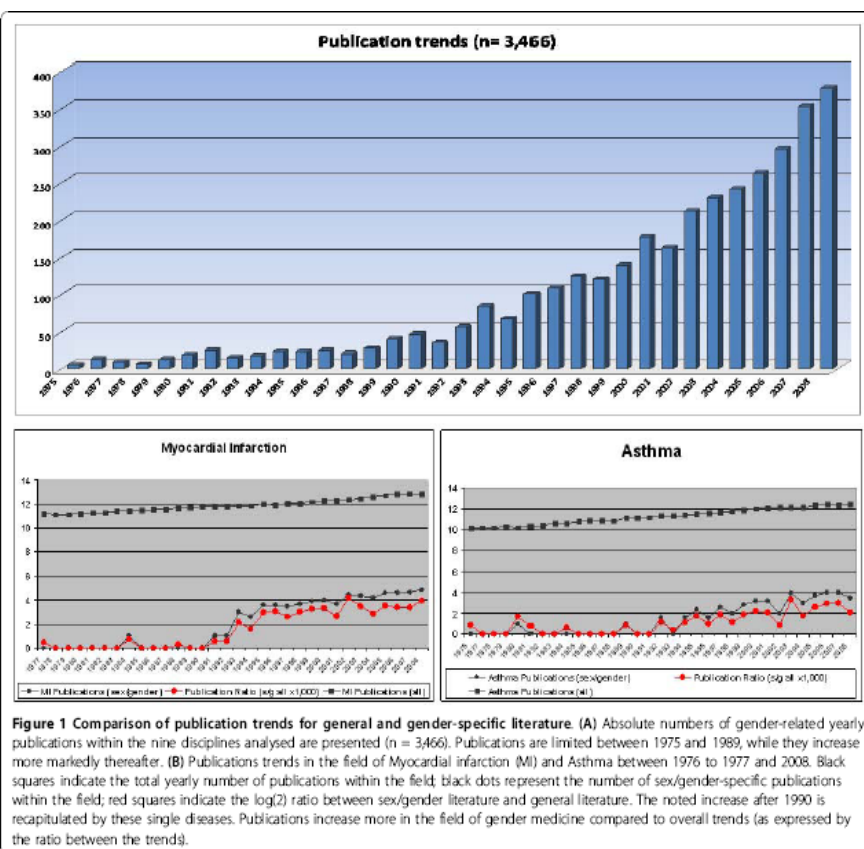


Figure 1 Comparison of publication trends for general and gender-specific literature. (A) Absolute numbers of gender-related yearly publications within the nine disciplines analysed are presented (n = 3,466). Publications are limited between 1975 and 1989, while they increase more markedly thereafter. (B) Publications trends in the field of Myocardial infarction (MI) and Asthma between 1976 to 1977 and 2008. Black squares indicate the total yearly number of publications within the field; black dots represent the number of sex/gender-specific publications within the field; red squares indicate the log₂ ratio between sex/gender literature and general literature. The noted increase after 1990 is recapitulated by these single diseases. Publications increase more in the field of gender medicine compared to overall trends (as expressed by the ratio between the trends).

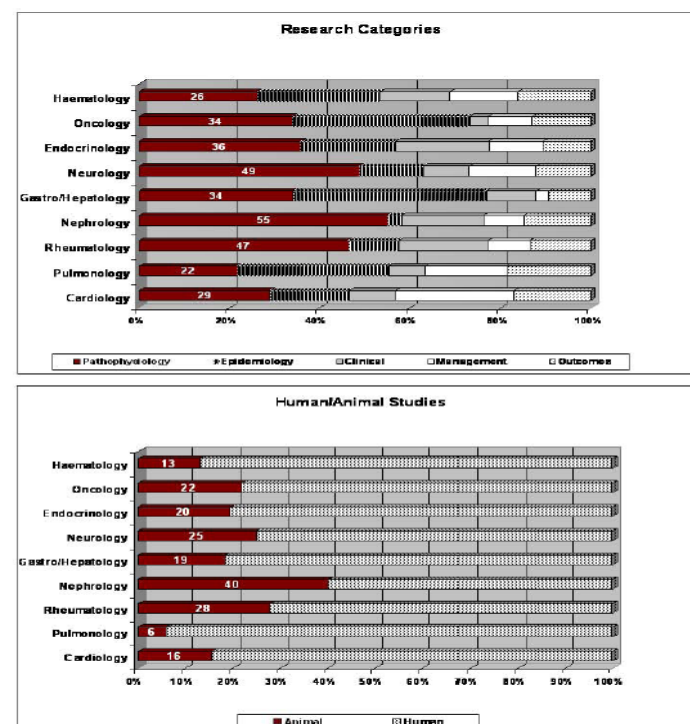
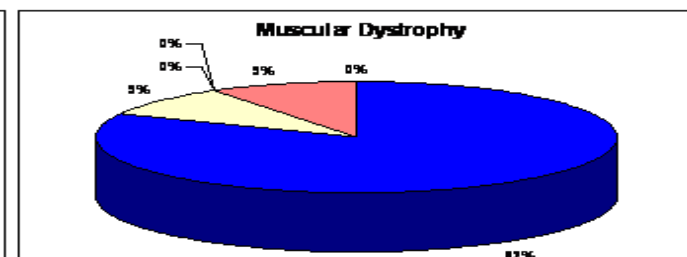
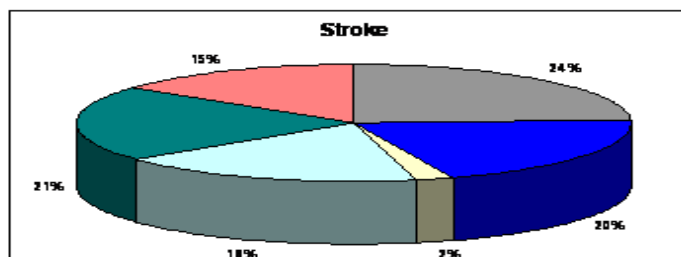
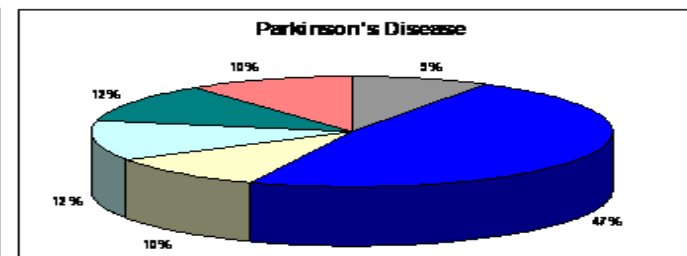
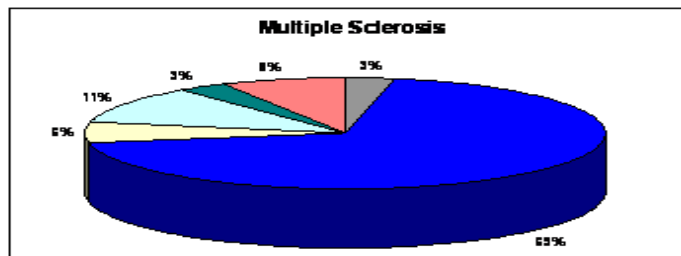
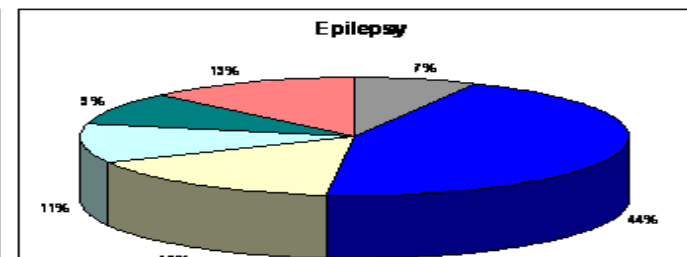
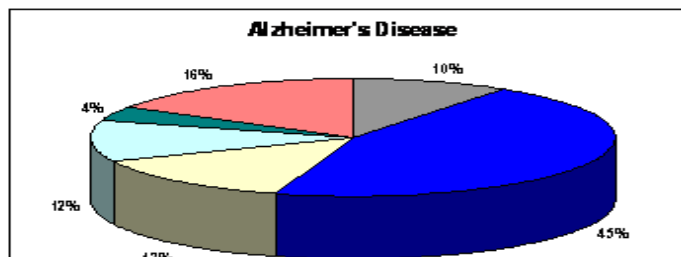
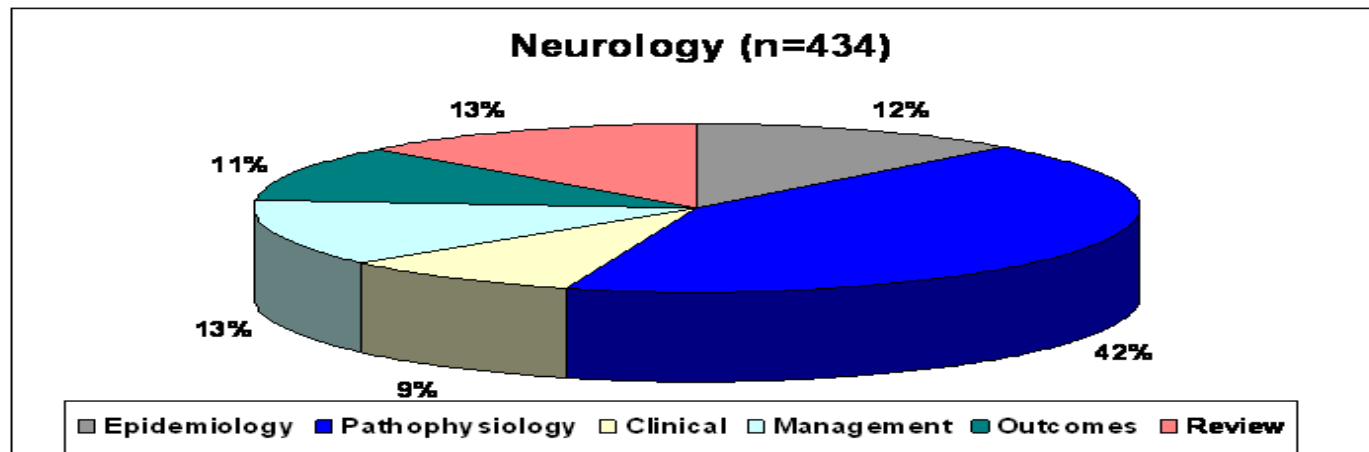


Figure 2 Analysis of gender-related publications. (A) Literature was classified into five research categories: Epidemiology, Pathophysiology, Clinical research, Management, and Outcomes. Research categories within the nine disciplines studied are illustrated. Equal distribution of research efforts would lead to a similar number of publications within each category. However, the categories of Pathophysiology and Epidemiology appear to be the most intensively investigated areas in most specialties. (B) The percentage of studies conducted on humans or animals was investigated. As all animal studies have been classified as "Pathophysiology" research, the relative percentages of animal model use can be derived by the ratio between the "Pathophysiology" data and the "Animal Study" data. Animal models are frequently used for basic research about sex differences; however, significant differences can be observed between specialties.



Le urgenze neurologiche nella donna in gravidanza

Congresso SIN 2008 Napoli

Riunione di consenso sulla sicurezza delle indagini neuroradiologiche in gravidanza

- Il parere del neurologo
- Il parere del fisico sanitario
- Il parere del neuroradiologo
- Il parere dell' ostetrico

Syllabi



delicato bilancio tra salute della madre e tutela del feto

ONDa

- Osservatorio Nazionale sulla salute della Donna

www.ondaosservatorio.it

- Bollini rosa



**Progetti innovativi per la salute della
donna G.Binetti
Congresso SIN Napoli 2008**



Medicina di Genere e misure di outcome orientate al paziente

Physician's
perspective:
DISEASE

Patient's
perspective:
ILLNESS

agreement?

Rothwell PM, et al. BMJ 1997; 314:1580-3

Programmi di indirizzo per la ricerca in Neurologia di Genere

- Cultura trasversale
- Integrazione multidisciplinare
- Linee guida con indicazioni di genere
- Indicazioni di genere e trattamenti individualizzati in ambito farmacologico
- Farmacovigilanza con strumenti bioinformatici (“data mining”)
- Osservatori epidemiologici con registri ospedalieri o di popolazione per analizzare l’impatto e l’interazione dei fattori di rischio delle malattie, le risposte i trattamenti, gli aspetti prognostici con raccolta di dati informativi su aspetti di genere (stratificazione)

Prospettive di sviluppo

- Estendere i concetti sulle **differenze** di genere in Neurologia in un ambito più moderno che comprenda la valutazione delle differenze di **etnia e culturalità**
- Favorire l' istituzione nella pratica clinica di attività organizzate con **teams multidisciplinari** dedicati alla **gestione della gravidanza** e di aspetti **ginecologici** in pazienti con malattie neurologiche
- Costituire partnerships con Aziende farmaceutiche e Fondazioni/Associazioni sensibili allo **sviluppo dello studio** degli aspetti Neurologici della Medicina di Genere
- **Collaborare** con le **Istituzioni** deputate alla **Formazione** ed al **Governo socio-sanitario** per favorire una ottica di genere per una medicina personalizzata **“diversity management”**

2 marzo 2012

Milano, Circolo della Stampa



Manifesto di Sex-Gender Medicine

Questo manifesto s'ispira a una serie di documenti internazionali, li integra con le esperienze italiane ed esplicita le azioni per migliorare la ricerca e l'innovazione, per sviluppare un cambiamento strutturale necessario per promuovere l'equità di genere.

- 1.** Ci sono solide ragioni scientifiche che evidenziano come le diseguaglianze di genere possano avere un impatto negativo sulla qualità della ricerca ed è evidente che, almeno in Europa, si è fallito nel sostenere e promuovere le donne nella stessa misura degli uomini: oggi in UE meno del 20% dei posti di ricercatore senior sono occupate dalle donne. La Commissione Europea e i politici italiani, pertanto, devono intraprendere iniziative per implementare l'entrata delle donne nelle posizioni apicali della scienza, inclusi i comitati che controllano l'erogazione dei fondi sia a livello privato che pubblico, nei comitati editoriali delle riviste ecc., per raggiungere l'equità di genere nella ricerca scientifica. Si potrebbe garantire, per esempio, che i singoli impegni di bilancio degli enti deputati alla ricerca anticipino i costi dell'integrazione della dimensione di genere come parte del progetto di ricerca e di processo.
- 2.** Promuovere una ricerca interdisciplinare e più bilanciata rispetto al genere e maggiormente basata su logiche di collaborazione in team abbandonando e/o modificando i modelli tradizionali deputati alla produzione di conoscenza per sviluppare un sistema collaborativo e cooperativo che accolga i diversi stili di leadership e adotti criteri di valutazione corretti rispetto al valore di tutte le persone coinvolte. Un'équipe di ricercatori di entrambi i generi migliora la qualità della ricerca, perché la ricchezza delle idee aumenta l'eccellenza scientifica e, l'intelligenza collettiva. Inoltre, la sensibilità di genere migliora le opportunità di stimolare il processo di ricerca basato sui bisogni degli uomini e delle donne.

2 marzo 2012

Milano, Circolo della Stampa

3. La ricerca interdisciplinare richiede di sviluppare criteri atti a valutare il lavoro interdisciplinare, poiché differenti discipline usano approcci e criteri diversi per definire l'eccellenza e ciò deve essere considerato in maniera da non costruire diseguaglianze fra le varie discipline.
4. Promuovere la ricerca su temi che portino benefici per entrambi i generi, anche perché aumentare la sensibilità di genere, significa migliorare e stimolare il processo di ricerca.
5. Le evidenze scientifiche differenze tra i due generi-sessi sono oramai numerosissime. Pertanto, per arrivare all'eccellenza della ricerca, i finanziatori, i valutatori, i revisori della ricerca ecc. dovrebbero chiedere ai ricercatori *“se e come, il fattore sesso-genere è rilevante negli obiettivi e nella metodologia del progetto”*.
6. Inserire il genere nei curricula studiorum a tutti i livelli per aumentare la consapevolezza degli operatori sanitari sul fattore sesso-genere.
7. Garantire che i prodotti e i servizi derivanti dalla ricerca siano efficaci e sicuri sia negli uomini sia nelle donne, si dovrebbe anche valutare se, come e quanto le differenze di sesso e di genere evidenziate siano rilevanti per la salute e la medicina, per fornire ad entrambi i generi la migliore cura possibile. Ai pazienti, agli operatori sanitari dovrebbe essere data la possibilità di accedere ai dati relativi alle differenze al sesso-genere, per migliorare la consapevolezza della diversità nell'uso dei farmaci, dei medical device e di altri approcci terapeutici. Costruendo anche specifici percorsi diagnostico terapeutici di sesso-genere.
8. Creare ambienti di lavoro flessibili e che supportino in modo equo le carriere di donne e uomini, affinché le specificità di genere siano ben gestite nei luoghi di lavoro per dare ad uomini e donne la possibilità di coniugare il loro lavoro alle aspirazioni di vita.
9. Promuovere incentivi per la ricerca di sesso-genere per arrivare all'equità della cura.

Settimana mondiale del cervello

dal 13 al 20 marzo 2012 con oltre 700 eventi in 39 nazioni e con un occhio puntato sul tema **‘Neurologia e donna’**, per una medicina di genere

- Info sul sito www.neuro.it.
- http://www.cybermed.it/index.php?option=com_content&task=view&id=30363&Itemid=134

The Precision Medicine Initiative (PMI) Working Group.

The Precision Medicine Initiative Cohort Program — building a research foundation for 21st century medicine.

Bethesda, MD: National Institutes of Health, 2015

(<http://www.nih.gov/precisionmedicine/09172015-pmi-working-group-report.pdf>).



The Precision Medicine Initiative Cohort Program – Building a Research Foundation for 21st Century Medicine

Precision Medicine Initiative (PMI) Working Group Report to the
Advisory Committee to the Director, NIH

September 17, 2015

Executive Summary

Precision medicine is an approach to disease treatment and prevention that seeks to maximize effectiveness by taking into account individual variability in genes, environment, and lifestyle. Precision medicine seeks to redefine our understanding of disease onset and progression, treatment response, and health outcomes through the more precise measurement of molecular, environmental, and behavioral factors that contribute to health and disease. This understanding will lead to more accurate diagnoses, more rational disease prevention strategies, better treatment selection, and the development of novel therapies. Coincident with advancing the science of medicine is a changing culture of medical practice and medical research that engages individuals as active partners – not just as patients or research subjects. We believe the combination of a highly engaged population and rich biological, health, behavioral, and environmental data will usher in a new and more effective era of American healthcare.



**LA MEDICINA DI GENERE:
UN NUOVO APPROCCIO ALLA SALUTE
E ALLE MALATTIE NEUROLOGICHE**

Medicina di genere e medicina di precisione
A. PROTTI (*Milano*)



Iscritti totali 1488 uomini e 1281 donne
ma tra i giovani 222 uomini e 505 donne

Coordinamento GdS: 2 donne su 16 GdS

Associazioni Autonome: 1 donna su 13 associazioni

Referee Congresso di Torino: 2011 12 donne su 98

Regione Lombardia

Convegno

LA SALUTE DELLA DIFFERENZA.

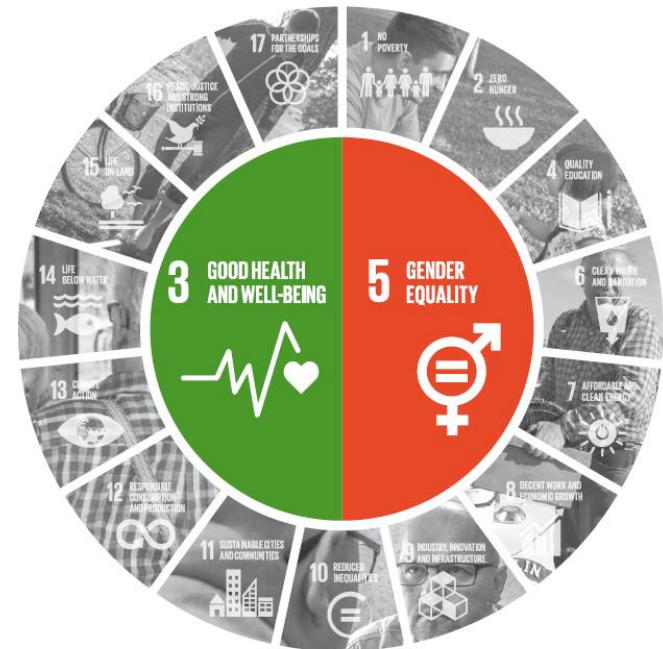
Politiche e orientamenti per la Medicina di
Genere

15 giugno 2012

Palazzo Lombardia, Milano



Women's health and well-being in Europe:
beyond the mortality advantage



The health and well-being of men in the WHO European Region:
better health through a gender approach



LETTER TO THE EDITOR

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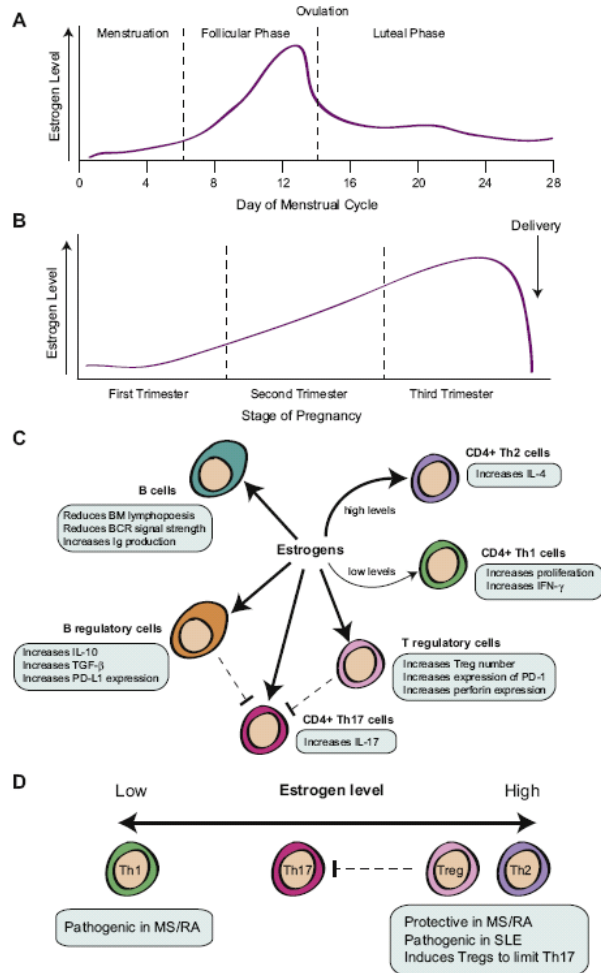
Preclinical studies of sex differences: a clinical perspective

Rhonda Voskuhl

Abstract

The new policy from the National Institutes of Health to encourage grant applicants to consider studying both females and males in preclinical biological experiments has been met with support and opposition. Here, we will discuss implications of preclinical studies of sex differences on clinical research.

Keywords: Sex differences, Translational research, National Institutes of Health



Contents lists available at SciVerse ScienceDirect

Journal of Autoimmunity

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



Review

Sex affects immunity

Leesa M. Pennell^{a,b}, Carole L. Galligan^{a,b}, Eleanor N. Fish^{a,b,*}

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ABSTRACT

Sex based differences in immune responses, affecting both the innate and adaptive immune responses, contribute to differences in the pathogenesis of infectious diseases in males and females, the response to viral vaccines and the prevalence of autoimmune diseases [1–5]. Indeed, females have a lower burden of bacterial, viral and parasitic infections, most evident during their reproductive years [2,6]. Conversely, females have a higher prevalence of a number of autoimmune diseases, including Sjogren's syndrome, systemic lupus erythematosus (SLE), scleroderma, rheumatoid arthritis (RA) and multiple sclerosis (MS). These observations suggest that gonadal hormones may have a role in this sex differential. The fundamental differences in the immune systems of males and females are attributed not only to differences in sex hormones, but are related to X chromosome gene contributions and the effects of environmental factors [7,8]. A comprehensive understanding of the role that sex plays in the immune response is required for therapeutic intervention strategies against infections and the development of appropriate and effective therapies for autoimmune diseases for both males and females. This review will focus on the differences between male and female immune responses in terms of innate and adaptive immunity, and the effects of sex hormones in SLE, MS and RA.



Review

Neuroprotective effects of estrogens and androgens in CNS inflammation and neurodegeneration

Rory D. Spence, Rhonda R. Voskuhl*

University of California, Los Angeles, Departments of Neurology, UCLA Multiple Sclerosis Program, 635 Charles E Young Drive South, Neuroscience Research Building 1, Room 479, Los Angeles, CA 90095, United States

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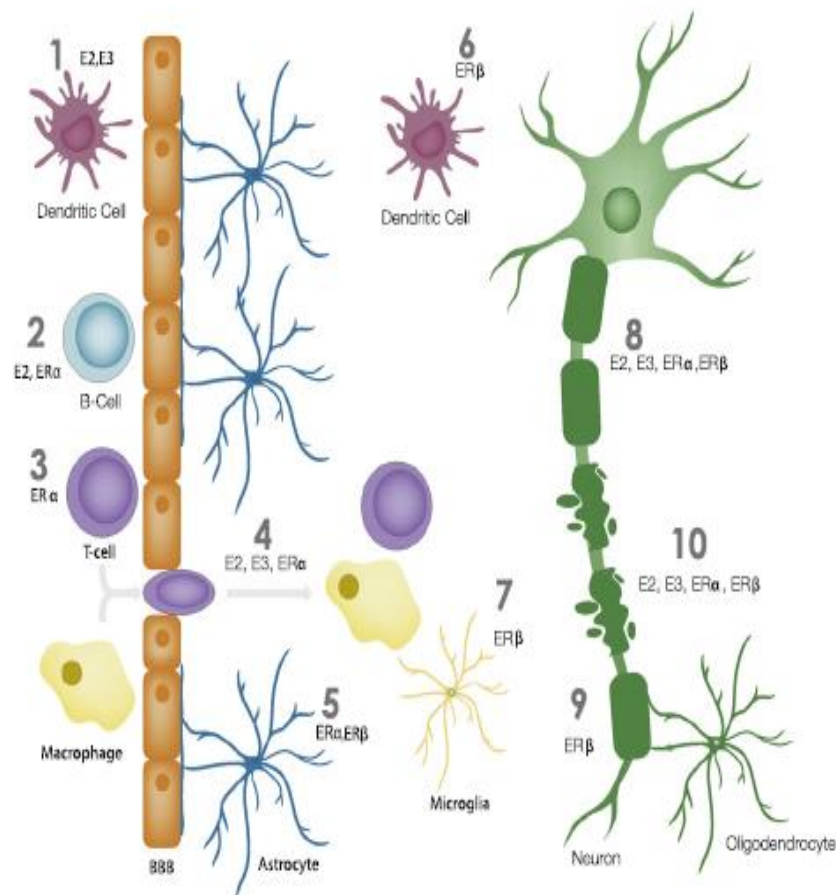
Keywords:

EAE
MS
ER α
ER β
Estradiol
Estradiol
Testosterone
SoDHT
Neuroprotection

ABSTRACT

Multiple sclerosis (MS) is a disease characterized by inflammation and demyelination. Currently, the cause of MS is unknown. Experimental autoimmune encephalomyelitis (EAE) is the most common mouse model of MS. Treatments with the sex hormones, estrogens and androgens, are capable of offering disease protection during EAE and are currently being used in clinical trials of MS. Beyond endogenous estrogens and androgens, treatments with selective estrogen receptor modulators (SERMs) for estrogen receptor alpha (ER α) and estrogen receptor beta (ER β) are also capable of providing disease protection. This protection includes, but is not limited to, prevention of clinical disease, reduction of CNS inflammation, protection against demyelination, and protection against axonal loss. In EAE, current efforts are focused on using conditional cell specific knockouts of sex hormone receptors to identify the *in vivo* targets of these estrogens and androgens as well as downstream molecules responsible for disease protection.

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A spotlight on sex differences in neurological disorders



Despite the importance of incorporating sex as a variable in experimental and clinical studies being recognised by the US National Institute of Mental Health already in 2011, and subsequently by other funding agencies in the USA and Europe, substantial evidence gaps exist for sex differences in the epidemiology, clinical features, and pathophysiology of many neurological disorders. In 2001, The Institute of Medicine, a branch of the National Academy of Sciences in the USA, formed a committee to explore current understanding of sex differences and the biological underpinnings of these differences in human health. Their report, which was a seed for the National Institutes of Health's broad commitment to account for the role of sex in health, identified barriers to progress in research on sex-based differences. Recommendations to address these challenges included that sex-specific data should be more readily available, longitudinal studies should be conducted so that the results can be analysed by sex, and interdisciplinary research on sex differences should be encouraged. Yet, challenges remain today.

In *The Lancet Neurology*, Linda Stephen and colleagues review the management of epilepsy in women, describing the unique issues due to hormonal changes and family planning. Data collection in epilepsy pregnancy registries is essential for informing the care of women receiving antiepileptic drugs. However, despite known antiepileptic drug interactions with steroid hormones, potential for teratogenicity, and worse pregnancy outcomes among women with epilepsy compared with those without, there is an absence of contraceptive counselling for many women with epilepsy and a gap in knowledge of the underlying causes for their increased morbidity and mortality during pregnancy.

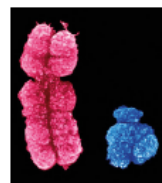
Family planning and pregnancy are pertinent issues across other neurological disorders as well, but the importance of data collection to inform neurologists on the safety of medications during pregnancy does not seem to have been consistently recognised. On Jan 5, 2019, consensus guidelines were published for the treatment of multiple sclerosis in pregnancy in the UK. While there are pregnancy registers in the UK specifically focusing on patients with multiple sclerosis taking dimethyl fumarate, teriflunomide, and alemtuzumab, the absence of large registry studies of the developmental outcomes of children

of women being treated for multiple sclerosis means that no comprehensive, up-to-date, central repository of information is available on best pharmacological management for these patients. The guidelines call for prospective data collection in a pregnancy register of all drugs and pregnancy-related outcomes in women with multiple sclerosis, pointing to the comparable role of epilepsy pregnancy registries.

The development of guidelines based on strong evidence needs not only prospective collection of data, but also a greater understanding of the implications of sex differences beyond family planning. In a Review of sex differences in migraine, while the safety of drugs in women with the disorder, in relation to contraception, pregnancy, and hormone replacement therapy, was identified as a priority to be addressed, the authors further underscored the potential for underdiagnosis of migraine in men because of a presumption that migraine is a female disorder. The predominance of women in clinical trials in migraine has led to a scarcity of data for men and thus suboptimal management. The authors note that treatment strategies do not differentiate between sexes, perhaps because the clinical trials informing practice did not adjust for sex.

A poor understanding of sex differences in neurological disease can lead to misconceptions and biases in management of male and female patients. Differences in management of stroke by sex have been discussed in another Review. The authors noted the importance of assessing sex differences in each aspect of the acute stroke evaluation process, but highlighted that differences in management strategies by sex are based on trials that have not been designed specifically to assess sex differences, have not adjusted for factors that might affect treatment and outcomes by sex, or were not adequately powered to identify sex-treatment interactions. Studies that have specifically aimed to evaluate sex as a modifier of outcome after treatment with thrombolysis have been inconclusive.

The recommendations of The Institute of Medicine in 2001 to facilitate research in sex differences and fill research gaps remain relevant today. Understanding sex differences should be a basic tenet of research from the mechanisms of disease to the clinical outcomes, to improve the diagnosis and management of neurological diseases for both sexes. ■ *The Lancet Neurology*



For The Institute of Medicine report see <http://www.nationalacademies.org/hmdj/-/media/Files/Report%20Files/2003/Exploring-the-Biological-Contributions-to-Human-Health-Does-Sex-Matter/DoesSexMatter03pages.pdf>
See Review *Lancet Neurol* 2019; published online March 8, [http://dx.doi.org/10.1016/S1473-4422\(18\)30495-2](http://dx.doi.org/10.1016/S1473-4422(18)30495-2)
For consensus guidelines on pregnancy in multiple sclerosis see *Pract Neurol* 2019; 0: 1-9
See Review *Lancet Neurol* 2017; 16: 76-87
See Review *Lancet Neurol* 2018; 17: 641-50

natureOUTLOOK

WOMEN'S HEALTH

5 October 2017 / Vol 550 / Issue No 7674



Preface

Women's Issues in Neurology

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¹ Division of Stroke, Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts

Semin Neurol 2017;37:599–600.

THE LANCET

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Advancing women in science, medicine, and global health

Gender equity is not only a matter of justice and rights, it is crucial for producing the best research and providing the best care to patients. If the fields of science, medicine, and global health are to hope to work towards improving human lives, they must be representative of the societies they serve. The fight for gender equity is everyone's responsibility, and this means that feminism, too, is for everybody—for men and women, researchers, clinicians, funders, institutional leaders, and, yes, even for medical journals.

— The Lancet

The February 9, theme issue on advancing women in science, medicine, and global health, contains new international evidence on forms of gender bias in funding; women's attrition in clinical training programmes; the extent to which universities worldwide have actualised their public commitments to gender and ethnic diversity; and the relationship between women's leadership in science and the production of sex/gender-related research.

New analysis and commentary establish the importance of feminist and masculinity theories, and problematise organisational strategies for increasing gender diversity in medicine and science. The importance of intersectionality, learning from the Global South, and the under-recognition of women's experience of harassment and abuse are key themes.

Collectively, the theme issue lays out robust evidence to inform an action plan for institutional leaders to confront gender bias, improve diversity and inclusivity, and drive change. Strategies to



Related content

Theme issue: read the content from *The Lancet's* Feb 9 issue, on advancing women in science, medicine, and global health.

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Feedback 💬

New horizons for future research — Critical issues to consider for maximizing research excellence and impact



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Contents lists available at ScienceDirect

Physiology & Behavior

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



Applying the new SABV (sex as a biological variable) policy to research and clinical care



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ARTICLE INFO

Keywords:

Sex differences
Policy
SABV
Rigor
Reproducibility

ABSTRACT

Sex as a biological variable (SABV) is a key part of the new National Institutes of Health (NIH) initiative to enhance reproducibility through rigor and transparency. The SABV policy requires researchers to factor sex into the design, analysis, and reporting of vertebrate animal and human studies. The policy was implemented as it has become increasingly clear that male/female differences extend well beyond reproductive and hormonal issues. Implementation of the policy is also meant to address inattention to sex influences in biomedical research. Sex affects: cell physiology, metabolism, and many other biological functions; symptoms and manifestations of disease; and responses to treatment. For example, sex has profound influences in neuroscience, from circuitry to physiology to pain perception. Extending beyond the robust efforts of NIH to ensure that women are included in clinical trials, the SABV policy also includes rigorous preclinical experimental designs that inform clinical research. Additionally, the NIH has engaged journal editors and publishers to facilitate reproducibility by addressing rigor and promoting transparency through scientifically appropriate sex-specific study results reporting. The Sex And Gender Equity in Research (SAGER) guidelines were developed to assist researchers and journal editors in reporting sex and gender information in publications [1].

J.A. Clayton

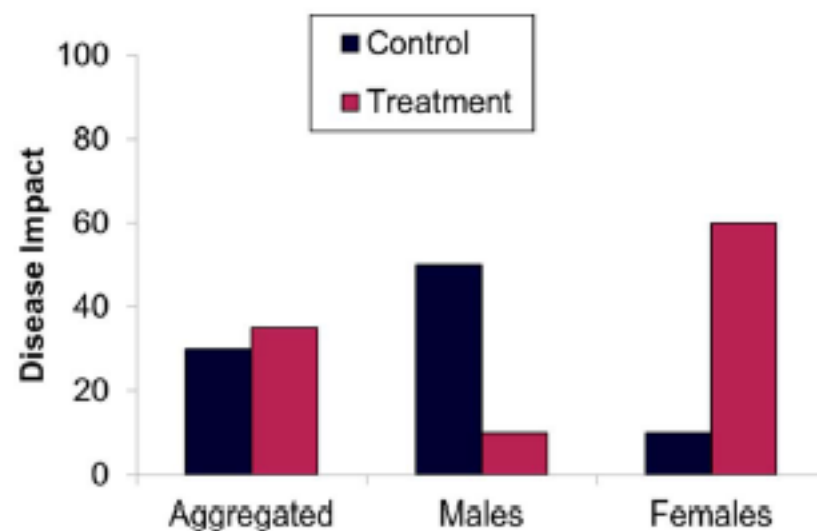


Fig. 1. Schematic diagram showing sex differences in disease impact similar to those reported by McCullough et al. [12]. In cases like this, important sex-by-treatment interactions can be masked when investigators only analyze data sets in which the two sexes are pooled. Disaggregating the data and considering the sexes separately can unmask important sex influences in laboratory animals or human subjects.

6. Conclusion

Sex and gender biomedical research extends far beyond the realm of reproductive health—it spans many diseases and conditions. It starts with differences at the cellular level, which extend through systems to the whole organism, i.e., to patients. Hence, considering the impact of sex at all levels of biology will help expand the knowledge base of male and female biology and inform appropriate individualized care for women as well as men. Accounting for SABV is the first step on the road toward personalized and ultimately precision medicine. To promote the most accurate and comprehensive science possible, the NIH policy to study sex as a biological variable entails that researchers consider sex in their study designs, collect data on both sexes unless there is justification not to, analyze the data accordingly, and report the results completely and transparently. Unless the effects of sex and gender are studied, we will continue to have gaps in the knowledge base, which may result in missed opportunities for discovery and better health. Having greater awareness of the roles that sex and gender play in health and disease will help the entire medical scientific enterprise achieve more clarity and enhance rigor and reproducibility.

SPREAD – Stroke Prevention and Educational Awareness Diffusion

Ictus cerebrale: Linee guida italiane di prevenzione e trattamento

Raccomandazioni e Sintesi

209



Il testo completo delle Linee Guida
è disponibile sul sito www.iso-spread.it
Codice QR Capitolo 17

MEDICINA DI GENERE

Sintesi 17.1

La patologia cerebrovascolare presenta un'elevata prevalenza nel genere femminile con peculiarità relative sia ai fattori di rischio che alle manifestazioni cliniche e agli outcome. Essa rappresenta una delle principali cause di morbidità e mortalità nella donna, tanto che le statistiche internazionali classificano l'ictus come la quinta causa di morte nel sesso maschile, ma la terza nel sesso femminile. Le proiezioni demografiche per il 2030 prevedono che circa il 20% della popolazione sarà rappresentato da soggetti di età superiore ai 65 anni con maggiore rappresentatività delle donne, in funzione dell'aspettativa di vita maggiore. Se consideriamo che circa la metà dei soggetti colpiti da ictus sopravvivono con quadri variabili di deficit funzionali e/o cognitivi, è possibile



Sex differences in the epidemiology, clinical features, and pathophysiology of migraine

Kjersti Grøtta Vetvik, E Anne MacGregor

Lancet Neurol 2017; 16: 76–87

Published Online

November 8, 2016

[http://dx.doi.org/10.1016/](http://dx.doi.org/10.1016/S1474-4422(16)30293-9)

[S1474-4422\(16\)30293-9](http://dx.doi.org/10.1016/S1474-4422(16)30293-9)

Department of Neurology and
Head and Neck Research Group,
Research Centre, Akershus
University Hospital, Lørenskog,
Norway (K G Vetvik PhD); and
Centre for Neuroscience and

Migraine is two to three times more prevalent in women than men, and women report a longer attack duration, increased risk of headache recurrence, greater disability, and a longer period of time required to recover. Conditions recognised to be comorbid with migraine include asthma, anxiety, depression, and other chronic pain conditions, and these comorbidities add to the amount of disability in both sexes. Migraine—specifically migraine with aura—has been identified as a risk factor for vascular disorders, particularly in women, but because of the scarcity of data, the comparative risk in men has yet to be established. There is evidence implicating the role of female sex hormones as a major factor in determining migraine risk and characteristics, which accounts for sex differences, but there is also evidence to support underlying genetic variance. Although migraine is often recognised in women, it is underdiagnosed in men, resulting in suboptimal management and less participation of men in clinical trials.

IMPATTO SOCIO-ECONOMICO DELL'EMICRANIA IN ITALIA

A cura dell'Istituto Superiore di Sanità
Centro di Riferimento per la Medicina di Genere



SINTESI

L'emicrania è una patologia di genere e sociale, con elevato impatto economico a carico dei pazienti che ne sono affetti e dei loro familiari

Le spese sono influenzate dal reddito



Gli uomini, che hanno redditi più elevati rispetto alle donne:

- sostengono spese più elevate per prestazioni sanitarie e non sanitarie
 - riportano maggiori perdite di produttività



Le donne rispetto agli uomini:

- hanno una sintomatologia peggiore con qualità di vita peggiore
 - perdono un maggior numero di giornate lavorative e di attività sociali/vita privata
- si recano più spesso al lavoro con dolore o malessere (presenteismo)

Delivery of a Personalized Treatment Approach to Women with Epilepsy

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Semin Neurol 2017;37:611–623.

Abstract

Personalized treatment for women with epilepsy is essential, and requires thorough weighing of the risks and benefits of the initial diagnostic and therapeutic options chosen, with readjustments of the antiepileptic regimen throughout the patient's life.

Approximately one-third of women with epilepsy have a catamenial pattern, and the most common pattern is an increase in seizure frequency in the perimenstrual phase. These women are also more likely to experience a decrease in seizure frequency during pregnancy and menopause. A good treatment option for catamenial epilepsy is still lacking.

For contraception, an intrauterine device is currently the preferred choice. Prior to conception, it is advisable to review the known impact of different antiepileptic drugs on the developing fetus and to optimize the patient's treatment regimen. Pregnancy registries and observational studies have provided key data and continue to refine our understanding of the risks to the structural and cognitive development of the fetus of specific antiepileptic drugs, including polytherapies and newer medications. Different studies consistently report that valproic acid has notably high relative risks for congenital malformations, lower IQ, and features of autism. During pregnancy, there is growing evidence that therapeutic dose monitoring is beneficial for seizure control. Counseling about seizure safety and minimizing provoking factors during the peripartum period is important for the patient with epilepsy.

Clinical studies continue to investigate the complex relationship between cycling sex steroid hormones, epilepsy, and antiepileptic medications, with hopes to better explain drug clearance changes during pregnancy, changes in seizure frequency, and neuroendocrine abnormalities. Thorough understanding of these key factors and a continuous review of literature for updated data on different treatment options will enable optimal treatment recommendations that will improve the health of women with epilepsy and their children.

Keywords

- epilepsy
- women's neurology
- women's health
- antiepileptic drugs
- catamenial epilepsy
- contraception
- pregnancy
- therapeutic drug monitoring
- menopause
- breastfeeding



Sex differences in autoimmune disorders of the central nervous system

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Received: 21 September 2018 / Accepted: 4 October 2018
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

Abstract

Stronger adaptive immune responses in females can be observed in different mammals, resulting in better control of infections compared to males. However, this presumably evolutionary difference likely also drives higher incidence of autoimmune diseases observed in humans. Here, we summarize sex differences in the most common autoimmune diseases of the central nervous system (CNS) and discuss recent advances in the understanding of possible underlying immunological and CNS intrinsic mechanisms. In multiple sclerosis (MS), the most common inflammatory disease of the CNS, but also in rarer conditions, such as neuromyelitis optica spectrum disorders (NMOSD) or neuronal autoantibody-mediated autoimmune encephalitis (AE), sex is one of the top risk factors, with women being more often affected than men. Immunological mechanisms driving the sex bias in autoimmune CNS diseases are complex and include hormonal as well as genetic and epigenetic effects, which could also be exerted indirectly via modulation of the microbiome. Furthermore, CNS intrinsic differences could underlie the sex bias in autoimmunity by differential responses to injury. The strong effects of sex on incidence and possibly also activity and progression of autoimmune CNS disorders suggest that treatments need to be tailored to each sex to optimize efficacy. To date, however, due to a lack of systematic studies on treatment responses in males versus females, evidence in this area is still sparse. We argue that studies taking sex differences into account could pave the way for sex-specific and therefore personalized treatment.

Sex bias in the immune system

Sex differences in CNS response to injury

Sex differences in incidence, activity,
and progression of CNS autoimmunity

Multiple sclerosis

Sex ratio in multiple sclerosis

Female multiple sclerosis patients have higher inflammatory
activity

Male multiple sclerosis patients have more pronounced
neurodegeneration



Contents lists available at ScienceDirect

Frontiers in Neuroendocrinology

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



A case for gender-based approach to multiple sclerosis therapeutics

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ARTICLE INFO

Keywords:

Multiple sclerosis

Gender

Sex

Sex differences

Clinical trials

Disease modifying therapies

Hormones

ABSTRACT

Despite established sex differences in multiple sclerosis (MS) risk and course, sex-specific efficacy and toxicity of existing MS therapies, and possible sex-specific therapeutic approaches, remain underexplored. We systematically reviewed published sex differences from Phase III pivotal trials for FDA or EMA-approved MS disease modifying therapies (DMTs), along with additional information from pharmaceutical companies, for pre-specified or *post-hoc* baseline characteristics, efficacy and safety outcomes by sex, and sex-specific concerns. Then, we reviewed trials testing hormonal therapies in MS. None of the Phase III clinical trials performed baseline sex-specific analyses or were powered to evaluate DMTs in menopausal/older populations. Some recent trials performed pre-specified or *post-hoc* stratification of outcomes by sex. Sex-specific hormonal intervention trials were limited. Adequately powered, pre-specified analyses accounting for baseline sex and age are required to maximize safety and efficacy in specific patient populations.

UK consensus on pregnancy in multiple sclerosis: 'Association of British Neurologists' guidelines

Ruth Dobson,^{1,2} Pooja Dassan,^{3,4} Megan Roberts,⁵ Gavin Giovannoni,^{2,6}
Catherine Nelson-Piercy,^{7,8} Peter A Brex⁹

Medicina di Genere

- Pronunciamenti ONU, UE, OMS
- Programmazione politiche sanitarie
- Obiettivi strategici PSN
- Priorità e metodologie della medicina di genere
- Incentivi fiscali per le industrie che producano ricerca di genere

- **Bando AIFA 2017** PER LA RICERCA INDIPENDENTE SUI FARMACI
Area tematica 3 – Medicina di genere
- **Legge Lorenzin 22 dicembre 2017:**
“Delega al Governo in materia di sperimentazione clinica dei medicinali, nonché disposizioni per il riordino delle professioni sanitarie e per la dirigenza sanitaria nel Ministero della salute”.



CRNI
Corsi Residenziali di Neuroimmunologia

17° CORSO CRNI

VIVA LA DIFFERENZA FEMMINILE

**VIVA LA DIFFERENZA:
SESSO & NEUROIMMUNOLOGIA**

Vive la différence: Sex & Neuroimmunology
Bergamo, Italy / March 7th – 10th 2018

**7 – 10 MARZO
2018**

**BERGAMO
ITALY**

PRESENTAZIONE DEL CORSO

Cari Colleghi,
è con rinnovato piacere che vi presento l'edizione 2018 dei Corsi Residenziali di Neuroimmunologia (CRNI), intitolata "Viva la differenza: sesso e neuroimmunologia". L'appuntamento è come sempre a Bergamo, dal 7 al 10 marzo 2018. Organizzato, come sempre, in stretta interazione con l'Associazione Italiana di Neuroimmunologia (AINI), il 17° Corso si occupa di uno dei temi più caldi della ricerca biomedica contemporanea: la medicina di genere. Il dimorfismo sessuale si riflette nello sviluppo del cervello e del sistema immunitario, così come nella loro interazione, in fisiologia e in patologia. Non si possono ignorare le marcate differenze di genere nell'ambito delle malattie autoimmunitarie del sistema nervoso, a partire dall'incidenza decisamente maggiore nel genere femminile, al decorso, alle conseguenze cliniche e di qualità della vita che le disfunzioni sessuali determinano, alla gestione della gravidanza. Come sempre, partiremo da nozioni di base per poi arrivare a dare nozioni che siano immediatamente spendibili nella pratica clinica quotidiana, insieme a indicazioni di dove il campo sta andando. Come sempre, il corpo docente è selezionatissimo sia per ciò che concerne le letture frontali che le tradizionali attività interattive, vero marchio di fabbrica dei CRNI.

Insomma, per restare al passo, non resta che rispettare la tradizione e partecipare anche quest'anno a un'edizione dei CRNI che prometta di essere all'altezza. Vi aspettiamo a Bergamo la prossima primavera.

Prof. Giancarlo Comi
Presidente dei CRNI

In copertina: Elizabeth Jameson & Joris Komen, *Mind in F*

<http://www.quadernidellasalute.it/quaderni-flipbook/26-aprile2016/index.php>



Rete di collaborazione per il sostegno della medicina di genere.

THE LANCET

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Advancing women in science, medicine, and global health

Gender equity is not only a matter of justice and rights, it is crucial for producing the best research and providing the best care to patients. If the fields of science, medicine, and global health are to hope to work towards improving human lives, they must be representative of the societies they serve. The fight for gender equity is everyone's responsibility, and this means that feminism, too, is for everybody—for men and women, researchers, clinicians, funders, institutional leaders, and, yes, even for medical journals.

— The Lancet

The February 9, theme issue on advancing women in science, medicine, and global health, contains new international evidence on forms of gender bias in funding; women's attrition in clinical training programmes; the extent to which universities worldwide have actualised their public commitments to gender and ethnic diversity; and the relationship between women's leadership in science and the production of sex/gender-related research.

New analysis and commentary establish the importance of feminist and masculinity theories, and problematise organisational strategies for increasing gender diversity in medicine and science. The importance of intersectionality, learning from the Global South, and the under-recognition of women's experience of harassment and abuse are key themes.

Collectively, the theme issue lays out robust evidence to inform an action plan for institutional leaders to confront gender bias, improve diversity and inclusivity, and drive change. Strategies to



Related content

Theme issue: read the content from *The Lancet's* Feb 9 issue, on advancing women in science, medicine, and global health.

Journal highlights: view selected content, organised by theme and published across the *Lancet* family of journals.

Launch events: read the programmes and watch the full #LancetWomen London and New York launches.

Profiles of women leaders: view the collection

International advisory group: read the members' biographies

Feedback 💬

www.eugenmed.eu/

- roadmap per l' inclusione degli aspetti di sesso e genere nella ricerca biomedica e sulla salute
- riconosce l' importanza di valorizzare gli aspetti di sesso e genere nella diagnosi, nel trattamento e ricerca delle malattie

Integrating topics of sex and gender into medical curricula-lessons from the international community

Biol Sex Differ. 2016 Oct 14;7 (Suppl 1):44

<https://www.ncbi.nlm.nih.gov/pubmed/27785346>

Nell'era della medicina personalizzata, è fondamentale, al fine di ottimizzare la cura del paziente, la formazione della prossima generazione di scienziati e operatori sanitari sulle differenze di sesso e di genere nelle malattie. In questo commentario sono riportati esempi di quanto è stato fatto in USA, Canada, Svezia e Germania per diffondere la medicina di Genere nell'educazione sanitaria e nei curricula universitari.

The Basic Science and The Biological Basis for Sex-and Gender-Related Differences

- Understanding the Importance of Sex and Gender in Biomedical Research
- Legislative Process Framework
- Cell Physiology
- Developmental Biology
- Pharmacodynamics and Pharmacokinetics
- Clinical Applications of Genomics

Sex and Gender Differences in Health and Behavior

- Clinical research methodology
- Endocrine effects on immunity
- Drug therapeutics during pregnancy
- Understanding the importance of sex and gender in mental health
- Autoimmunity, autoimmune disease, and sex bias
- Sex and gender differences in irritable bowel syndrome

The Influence of Sex and Gender on Disease Expression and Treatment

- Sexual Dimorphism in Metabolic Bone Disorders
- Cardiovascular Disease in Women: A Focus on Heart Failure
- Sex and Gender Differences in Pulmonary Function and Health
- The Neural Basis of Sex Differences in Pain
- Sex Differences in Substance Abuse and Treatment

<https://sexandgendercourse.od.nih.gov>

A string for the gender-specific medicine universe

Ital J Gender-Specific Med 2016; 2(1): 42-44

Go to <http://www.sexandgenderhealth.org/resources.html> where you will be directed to PubMed by selecting

1. The **Basic Search** String:
(sex based OR sex factors OR sex distribution OR sex characteristics OR sex dimorphism OR gender difference* OR gender based) AND (gender[ti] OR sex[ti]) AND (Humans[Mesh] AND English[lang])
2. Or the **Advanced Search** String:
(sex based OR sex factors OR sex distribution OR sex characteristics OR sex dimorphism OR gender difference* OR gender based) AND (gender[ti] OR sex[ti] OR women[ti] OR female[ti]) AND (Humans[Mesh] AND English[lang])

Once you are on the PubMed website, having selected, for example, Basic Research String, if you wish to perform an even more specific search, click Advanced.

On the screen shown here click Add next to #1.

The search string will appear on the first line of the Builder section. Restrict your search to your fields of interest using the lines in the Builder section, using the various options available, for example, AND cardiovascular. It is possible to continue restricting the research in the cardiovascular field even further by adding, for example, AND elders. And so on, to continue to further narrow the search field. At the end, click Search and all the articles relevant to the search performed will appear. To perform other searches or restrict the search further, click Advanced and follow the instructions provided.

[http://ec.europa.eu/programmes/horizon
2020/en/h200-section promoting-gender-equality-
research-and innovation](http://ec.europa.eu/programmes/horizon2020/en/h200-section_promoting-gender-equality-research-and_innovation)

www.eugenmed.eu/

- roadmap per l' inclusione degli aspetti di sesso e genere nella ricerca biomedica e nella salute
- riconosce l' importanza di valorizzare gli aspetti di sesso e genere nella diagnosi, nel trattamento e ricerca delle malattie

Chi sono gli attori che possono maggiormente favorire lo sviluppo della Medicina di Genere?

Ministero della Salute e Istituto Superiore di Sanità
Regioni (Assessorati della salute)
Agenzia Italiana del farmaco (AIFA)
Società Scientifiche

Regioni (Programmazione)
Medici di Medicina Generale
European Medicines Agency (EMA)
Industria
Associazioni Pazienti
Ministero Università
Media

- Bando AIFA 2017 PER LA RICERCA
INDIPENDENTE SUI FARMACI

Area tematica 3 – Medicina di genere

- Legge Lorenzin 22 dicembre 2017:
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clinica dei medicinali, nonché disposizioni per il riordino
delle professioni sanitarie e per la dirigenza sanitaria nel
Ministero della salute”.**



WORKSHOP

ore 15.00 - 17.00

LE URGENZE NEUROLOGICHE IN GRAVIDANZA: ORGANIZZAZIONE DEI PERCORSI DI CURA

Moderatori

G. GIUSSANI (*Milano*) - A. PROTTI (*Milano*)

- 15.00 **La gestione delle urgenze tra territorio e ospedale**
R. ZANINI (*Lecco*)
- 15.30 **Le emergenze neurochirurgiche e neurointerventistiche**
M. PIANO (*Milano*)
- 16.00 **La cefalea acuta nella donna gravida**
G. BONO (*Pavia*)
- 16.30 **Presentazione del volume: Neurological Emergency during Pregnancy**
A. PROTTI (*Milano*)

organizzazione dell'offerta
dei servizi sanitari
dedicati all'assistenza di donne
con patologie neurologiche

-assistenza -formazione -ricerca



Centri “esperti”
Rete Hub & Spoke

Special Topic Section: Sex and Gender in Alzheimer's Disease

Understanding the impact of sex and gender in Alzheimer's disease: A call to action

Table 2

Research priority areas in sex and gender differences in AD clinical research

Further investigation of:

1. The extent to which findings of sex and gender differences in AD are due to differences in longevity, survival bias, and comorbidities
2. Potential sex-specific risk factors for AD (e.g., oophorectomy, menopause, pregnancy, androgen-deprivation therapy, and testosterone loss) across the life span
3. The influence of estrogens and hormone therapy on brain function and AD risk in light of discrepancies in the clinical literature
4. Potential sex differences in genetic risk factors for AD (e.g., APOE, x-linked, common variants, autosomal dominant mutations, and so forth)
5. Sex and gender differences in AD risk factors that are observed in both sexes (e.g., cardiovascular disease, diabetes, education, depression, and so forth) across the life span
6. Sex differences in AD progression and the trajectory of change in cognitive function, neuroimaging, CSF, and blood-based biomarkers of AD
7. The effects of sex differences in brain development on sex differences in brain aging and, ultimately, AD pathology and dementia
8. The effects of sex and gender in risk factors, disease progression, and biomarkers in racial and ethnic subgroups, especially in African Americans and Hispanics/Latinos, and how this informs differential risk
9. The factors involved in the secular changes (e.g., societal, political) and geographical variation in estimates of sex differences in AD
10. Gender differences in caregiving and how the burden of caregiving influences AD risk
11. Sex and gender differences in developing AD therapeutics, from preclinical to clinical studies, and in the design of clinical trials
12. The effects of sex and gender differences on the clinical detection, diagnosis, management, and treatment of AD for both sexes

Abbreviations: AD, Alzheimer's disease; APOE, apolipoprotein E; CSF, cerebrospinal fluid.

Consideration of Sex Differences in Medicine to Improve Health Care and Patient Outcomes

Marianne J. Legato, MD
Columbia University,
College of Physicians
and Surgeons,
New York City, New York.

Paula A. Johnson, MD, MPH
Wellesley College,
Wellesley, Massachusetts.

JoAnn E. Manson, MD, DrPH
Connors Center for
Women's Health and
Gender Biology,
Brigham and Women's
Hospital, Harvard
Medical School,
Boston, Massachusetts;
and Harvard T.H. Chan
School of Public Health,
Boston, Massachusetts.

Box. Sex Differences in Metabolism and Cardiovascular Disease

Sex Differences in Medications

Women have higher blood concentrations of propranolol, zolpidem, digoxin, and other medications, when given a standard dose.

Adverse effects of angiotensin-converting enzyme inhibitors (cough) and statins (myalgias and diabetes risk) are more common in women than in men.

Risks of major bleeding with tissue plasminogen activator and warfarin are higher in women than in men.

Aspirin tends to lower risk of stroke in women and myocardial infarction in men.

Sex Differences in Cardiovascular Disease

Women have higher risks for atrial fibrillation–associated stroke, stroke-related mortality, and risk of atrial fibrillation recurrence following ablation.

Women's longer cQT interval increases risk of torsades de pointes with several medications, including sotalol, amiodarone, dofetilide, aximilide, and some antihistamines.

Most coronary artery disease risk factors are similar in men and women but diabetes is a stronger risk factor in women.

Women are more likely to have dyspnea or other atypical symptoms of myocardial infarction (and are less likely than men to report chest discomfort).

Standard stress tests have lower sensitivity and specificity in women: stress echocardiography is preferred for women.

Women may have a higher risk frequency of vascular spasm, microvascular disease, or both.

Takotsubo disease occurs almost exclusively in women.

Heart failure due to diastolic dysfunction (preserved ejection fraction) is more common in women than in men.

JAMA Published online October 31, 2016

Grazie per l'attenzione

