Is gender meaningful for research?

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WE HAVE STUDIES OF FRUIT FLIES, MICE, HAMSTERS, FROGS, MONKEYS AND MEN WITH THIS CONDITION - BUT MEDICAL RESEARCH USING WOMEN AS SUBJECTS JUST NEVER OCCURRED TO ANYBODY.
Prototype of normalcy

White men,
1,80 m, 70 Kg,
Wanted for clinical research

Historical blindness, need to study homogenous samples, even female rats were excluded from research
The « gender gap » in clinical research

- Women have been under-represented in clinical biomedical research: inhomogenous group
- Gender related analysis is reported in only 24% of cardiovascular studies
- The datas observed in male subjects are extrapolated in females.
- No specific recommandations for women until recently (2013)
- Although this has been discussed for several years, recruitment is still insufficient
- Asymmetry of knowledge in pathophysiology

Healy, JAMA 1991; 266:566
The « gender gap » in cardiovascular research

• The first cause of death in women is cardiovascular disease: 54% (23% cancer).
• Yet, women receive less cardiovascular investigation and treatment than men (false myths, breast angina is benign in women)
• Diagnosis is more difficult: thallium non validated in women, coronarography is aspecific
• Women with cardio-vascular attacks receive less intensive treatment (angioplasty, bypass) and cardiac rehabilitation than men.
Examples of exclusion

- MRFIT: cardiovascular risk factors and mortality 12,866 men
- Physician Health Study: aspirin on CV risk 22,000 men
- HAPPHY: Cv mortality, 6,569 men
- HHS: Cv mortality, 4,081 men
- Association between coffee and cardiovascular risk: 44,000 men
- AMIS: 11% women; ISIS-II: 30% women; TIMI-II: 14% women; GISSI-2: 20% women
- Women receive less evidence-based treatment than their male counterparts

Worse outcomes for women in acute myocardial infarction

- Atypical and delayed presentation
- Treatment bias - less invasive procedures and revascularisation therapies. Inferior secondary prevention
- More co-morbidities and older age
- Biological bias - Different response to anti-platelet agents and smaller vessels
- Assessment bias - Less access to intervention and more delays in referrals
Atypical... Growing medium

Grand-mother treated the village with plants, Valle d’Aosta, Italia

Father created an Agriculture Museum, Chiblins

Grand father was a hunter poacher

- No University diploma in family
- Farmer medium
- No piston
Thanks to Prof. Francis Waldvogel

Pr Nanette Wenger, Emory, Atlanta, NIH conference

• N. Wenger: among the first physicians to focus on coronary heart disease in *women*, and to evaluate the different risk factors and features
• In a legendary career that spans more than 50 years, Dr. Wenger’s steadfast dedication to reducing women’s disability and death from cardiovascular disease
• chaired the U.S. National Heart, Lung, and Blood Institute Conference on Cardiovascular Health and Disease in Women

Wenger NK: Cardiovascular effects of raloxifene: The potential for cardiovascular protection in women. *Diabetes, Obesity, & Metabolism* 2002;4:166–176
Starting my clinical research, I focused on link between the sex female hormones and the kidney, the blood pressure regulation and the salt-sensitivity in women.
Starting my clinical research

• Hans Brunner’s team CHUV, wrote the history of the renin-angiotensin-aldosterone system.
• Realized: Women and female animals underrepresented in research
• Clinical science and health care are less evidence based for women than men.
• Starting my clinical research, I was interested in kidney disease, and especially blood pressure regulation.
• I designed studies in order to assess salt handling and interaction with sex female hormones.
Orthostatic hypotension in women, negative « picture » of hypertension: nocturnal renal escape of sodium
• Effect of sodium on the renal hemodynamics in women on various hormonal states (2 phases of menstrual cycle, contraceptives, menopause, pregnancy), and studies of the complete sodium of tubular renal handling

Pechère Bertschi et al, Clinical Science 2000; 98:697
Endogenous and exogenous effect of sex female hormones on pressure-natriuresis curve

$U_{Na} \cdot V$ (mmol/d)

- follicular
- luteal
- contraceptive
- menopause
- preeclampsia

Martillotti, Pechère-Bertschi, Hypertension 2013
Preeclampsia and hypertensive disorders of the pregnancy

- Hypertensive disorders (preeclampsia) of the pregnancy are a major cause of maternal morbidity and mortality (38%).
- One woman deceases each 7 minutes from a pregnancy related hypertensive trouble worldwide.
- Most frequent medical disease of the pregnancy (~15%), (preeclampsia 3-10%, black people prone).
- Expected to increase because of the epidemic augmentation of diabesity (diabetes and obesity) in developed and developing countries.
Renal Post-pre-eclampsia project
A. Pechère, A. Ditisheim, G. Wuerzner, M. Boulvain, M. Burnier, O. Irion

- Prospective observational cohort study (genetics, plasma date bank) with long term renal impairment and cardiovascular disease follow-up
- Case control-study examining the renal markers in the post partum vs control group
- A randomized, double-blind, placebo controlled trial examining the efficacy and safety of blockade of the renin system on renal endpoints
- Consultation of preeclampsia
What does help

- The right mother in law
- The right husband
- An athletic physics
- A small need to sleep
- Marathonien mental
- La qualité de l’entourage

What does not help

- Not to be able networking
- Absence of model and menthor
- Feeling guilty
- Perfectionism
- Not to be able to delegate
A gender bias in my family

« ..I have not felt absenteeism from you. I knew you were here for me. You were right to do it, if it is good for you.. »

Benoît, medical student 3e year

« ..the fact that you were working did not cause any emotional deprivation.. It was normal for me.. »

Laurent, Master in Economics and statistics Bern and Toronto,

« ..you are a model for me, I am proud of you, and I would like to do the same. I never felt any emotional or any deprivation »

Nicolas, medical student 3y, (1990-2013)

A gender bias in my family
Thanks

• The dean Pr Henri Bounameaux
• The Commission of Egality (Faculty of Medicine)
• Michel Burnier, Hans Brunner, Francis Waldvogel, Hans Stalder, Alex-F Müller, Michel Leski….