

Women and respiratory disease – a sex and gender perspective

Over the past decade there has been a growing literature about the complex issues of sex and gender and their interaction in respiratory disease expression as well as in clinical recognition and management. Despite the evidence that both sex (the biology) and gender (the socially constructed roles and activities) impact on disease susceptibility, expression, recognition and management in primary care, international guidelines frequently fail to include this information.

Airway response to toxins (cigarette smoke, biomass fuels, environmental pollutants) differs by sex,¹ based on the effects of female hormones on lung development and size, on regulation of receptors and biochemical pathways and on airways' hyper responsiveness and inflammation. These differences appear to increase the susceptibility of post-pubescent girls and women to asthma, COPD and lung cancer,^{2,5} as well as some respiratory infections,⁶ and infiltrative lung diseases.^{7,8} In addition, gender (social roles) exposes girls and women to higher levels of toxins from biomass fuel used for cooking, and to particular occupational and chemical triggers. Women may have differences in symptom expression, disease progression and co-morbidity patterns (e.g. depression and osteoporosis). This, together with our failure to ask necessary questions about symptoms, may partially explain the gender bias in diagnosis of respiratory diseases.^{9,10}

This desktop helper addresses the key points related to sex and gender differences in the identification, diagnosis and care of respiratory disease in girls and women.

SMOKING

In many countries women's smoking rates are increasing, especially in young women.¹¹ Targeted marketing presents smoking to girls and women with powerful messages of glamour, independence and weight and mood control.¹² Recent

systematic reviews show a greater loss of lung function in female than male smokers by age.¹³ Moreover women appear to be more susceptible to the effects of tobacco in lung disease initiation and progression, especially in COPD and cancer.^{2,3,13,14}

Women may be less likely to disclose smoking behaviour and health professionals are less likely to ask non-pregnant girls and women about smoking and secondhand smoke exposure.¹⁵⁻¹⁷

Practice tip: So always ask about smoking - and also ask about passive smoking.

Smoking cessation, the most significant intervention to slow the rate of lung function decline, has an even clearer advantage for women than it does for men.¹⁸ Yet women smokers have more relapses¹⁹ and may have higher levels of nicotine dependence and more depressive and withdrawal symptoms.²⁰

Practice tip: Tailor cessation advice, include gender specific issues (especially weight gain) and consider prescribing and counselling.

COPD

The worldwide prevalence of COPD is growing faster among women than men in many countries. COPD-related hospitalization and mortality rates are higher among women in the USA where, since 2000, more women than men die each year of COPD.²¹

The latest evidence shows that women are more likely than men to develop the bronchitic COPD phenotype rather than the emphysematous one, for reasons that still remain unclear.^{14,22,23} The roles of known sex difference in a number of biological markers and autoimmune activity in the development and progression of COPD continue to be studied. In women with a history of smoking or biomass fuel exposure the suspicion of COPD must remain high. Women with COPD report more dyspnoea and, at matched FEV₁, have a higher degree of dyspnoea,^{23,24} and less sputum.²⁵

However, even when reporting exactly the same symptoms as men, women are less likely to be diagnosed with COPD, but with asthma.¹⁰

Practice tip: Women may not experience typical COPD symptoms, so maintain a high index of suspicion and active enquiry. Reassess new diagnosis of asthma in older women. Is it really mixed disease or COPD?

Studies using hypothetical cases have shown that given the same symptoms, primary care doctors are less likely to consider a diagnosis of COPD in women. When spirometry results were added, the diagnosis was less likely to be overlooked.^{10,23,26}

Practice tip: Consider COPD in all women patients with a smoking history or chronic biomass fuel use exposure and any chronic respiratory symptoms. Spirometry and objective evidence helps in overcoming bias. (See IPCRG Desktop Helper 5 for tips on early diagnosis)

COPD may have more rapid progression in women, with greater dyspnoea and less activity tolerance for the same level of lung function compared to men, resulting in lower quality of life for women with COPD.^{5,27,28} Women with COPD have also higher levels of depression, anxiety and osteoporosis but a lower likelihood of cardiovascular co-morbidities which is the cause of their lower mortality compared with men, despite a worse general clinical picture.^{5,24,28}

ASTHMA

The pattern of asthma increasing in girls after puberty is based in part on the influence of sex hormones on its inflammatory pathophysiology. Asthma is 20% more frequent in women than men over the age of 35.²⁹ Hormonal changes may affect asthma during pregnancy, and at specific times during the menstrual cycle.^{4,30} Women may also have gender-related increased exposure to household, occupational, fragrance and cosmetic-related chemical triggers, but also psychological ones.^{30,33} Use of biomass and solid fuels also increases asthma risk.³⁴

◀ **Practice tip:** Trigger assessment is important in achieving asthma control and should include gender-specific considerations. Psychological stress as well as smoking³⁵ should also be explored as a trigger.

Women with asthma have a more positive attitude towards their medication, have a higher reported adherence, and use inhaled corticosteroids more often than men.^{36,38} At the same time women report more often anxiety and insomnia than men.³⁶ Depression may contribute to increased asthma symptoms or severity.³⁹ Little work has been completed on sex differences in quality of inhaler and peak flow meter (PFM) technique, which would appear better in men than in women, even though in the case of inhalers, spacer use could reduce the difference. Both techniques should be reviewed periodically.^{37,38,40,41}

There is evidence that management approaches that take into account sex and gender role factors may result in improved health status, reduced rescue medication use and improved QOL.⁴²

Practice tip: Take your time to talk with the patient, thinking about sex and gender issues as well as co-morbidities that may affect her self management e.g. carer responsibilities that might delay care seeking.⁴³

OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)

OSAS is more common in men than women, and biological differences are important in anatomy variations, obesity patterns and breathing control. Given equal BMI and age, women have more frequent sleep interruptions and a greater number of OSAS episodes in the REM phase.⁴⁴ Yet men are more likely to be diagnosed or referred for further investigation of OSAS.⁴⁵

Practice tip: Talk to women and their partners about snoring and daytime sleepiness to assess the possibility of OSAS.

LUNG CANCER

Since the 1950s, lung cancer prevalence among women has increased worldwide by 500%.⁴⁶ Since 1996 lung cancer mortality in women has surpassed annual breast cancer

mortality⁴⁷ while lung cancer mortality rates have been decreasing in men.^{3,48,49}

Practice tip: Like COPD, lung cancer is not a disease of old men. Add COPD and lung cancer to your differential diagnosis of respiratory symptoms in women smokers and those exposed to biomass fuel use.

REFERENCES

- Clougherty JE. Environmental Health perspectives 2010
- Kiyohara C, Yoshiyuki O. Sex differences in Lung Cancer Susceptibility: A Review. *Gender Medicine: The Journal for the Study of Sex & Gender Differences* 2010;7(5):381-401.
- Baldini EH, Strauss GM. Women and Lung Cancer: Waiting to Exhale. *Chest* 1997;112 [4 Suppl]:229S-234S.
- Balzano G et al. Asthma and sex hormones. *Allergy* 2001;56:13-20.
- Lavolette L et al. Chronic obstructive pulmonary disease in women. *Can Respir J* 2007;14(2):93-8.
- Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. *Tuber Lung Dis* 1996;77(5):391-400
- Kitaiichi M, Nishimura K et al. Pulmonary lymphangioleiomyomatosis: a report of 46 patients including a clinicopathologic study of prognostic factors. *Am J Respir Crit Care Med* 1995;151:527-33.
- Adamson D, Heinrichs W et al. Successful treatment of pulmonary lymphangioleiomyomatosis with oophorectomy and progesterone. *Am Rev Respir Dis* 1985;132:916-21 98
- Ruiz-Cantero MT, Ronda E, Alvarez-Dardet C. The importance of study design strategies in gender bias research: the case of respiratory disease management in primary care. *J Epidemiol Community Health* 2007;61:11-16.
- Chapman KR, Tashkin DP, Pye D. Gender Bias in the Diagnosis of COPD. *Chest* 2001;119:1691-5.
- The Tobacco Atlas, WHO
- Ernster V, Kaufman N, Nichter M, Samet J, Yoon SY. Women and tobacco: moving from policy to action. *Bull WHO* 2000;78(7):891-901.
- Sorheim IC, Johannessen A, Gulsvik A, Bakke PS, Silverman EK, Demeo DL. Gender Differences in COPD: are women more susceptible to smoking effects than men? *Thorax* 2010;65:480-5.
- Prescott E, Bierig AM, Andersen PK, Lange P, Vestbo J. Gender difference in smoking effects on lung function and risk of hospitalization for COPD: results from a Danish longitudinal population study. *Eur Respir J* 1997;10:822-7.
- Greaves IJ, Richardson IA. Tobacco Use, Women, Gender, and Chronic Obstructive Pulmonary Disease: Are the Connections Being Adequately Made? *Proc Am Thorac Soc* 2007;4(8):675-9.
- Zerbe, K. (1999) *Women's Mental Health in Primary Care*. Saunders Company, Philadelphia
- Lumley J, Chamberlain C, Dowswell T, Oliver S, Oakley L, Watson L. Interventions for promoting smoking cessation during pregnancy. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD001055. DOI: 10.1002/14651858.CD001055.pub3
- Connett JE, Murray RP, Buist AS, Wise RA, Bailey WC, Lindgren PG, Owens GR. Lung Health Study Research Group. Changes in smoking status affect women more than men: results of the Lung Health Study. *Am J Epidemiol* 2003;157(11):973-9.
- U.S. Surgeon General. The health consequences of smoking: a report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, Office of the Surgeon General; 2004.
- Langhammer A et al. Cigarette smoking gives more respiratory symptoms among women than among men. The nord-Trøndelag Health Study (HUNT). *J Epidemiol Community Health* 2000;54(12):917-22.
- Han MK et al. Gender and Chronic Obstructive Pulmonary Disease: Why it matters. *Am J Respir Crit Care Med* 2007;176(12):1179-84.
- Martinez FI. Sex differences in severe pulmonary emphysema. *American Journal of Critical Care Medicine* 2007;176:243-8.
- Chapman KR. Chronic obstructive pulmonary disease: are women more susceptible than men? *Clin Chest Med* 2004;25(2):331-41.
- De Torres JP et al. Gender Differences in Mortality in Patients with COPD. *ERJ Express* 2008;2:29.

- Celli B et al. Gender Differences in Mortality and Clinical Expressions of Patients with COPD: The TORCH Experience. *Am J Respir Crit Care Med* 2010;181:131.
- Miravilles M, de la Roza C, Naberan K, Lamban M, Gobarrt E, Martin A. Use of spirometry and patterns of prescribing in COPD in primary care. *Respir Med* 2007;101(8):1753-60. Epub 2007 Apr 19.
- De Torres JP, Casanova C, Hernandez C, Abreu J, Montejo de Garcini A, Aguirrejaime A, Celli BR. Gender associated differences in determinants of quality of life in patients with COPD: A case series study. *Health Qual Life Outcomes* 2006;4:72.
- Laurin C, Lavoie KL, Bacon SL, Dupuis G, Lacoste G, Cartier A, Labrecque M. Sex differences in the prevalence of psychiatric disorders and psychological distress in patients with COPD. *Chest* 2007;132:148-55.
- Leynaert B, Sunyer J, Garcia-Esteban R, et al. Gender differences in prevalence, diagnosis and incidence of allergic and nonallergic asthma: a population-based cohort. *Thorax* 2012. [Epub ahead of print]
- Carey MA, Card JW, Voltz JW, Arbes SJ Jr, Germolec DR, Korach KS, Zeldin DC. It's all about sex: gender, lung development and lung disease. *Trends Endocrinol Metab* 2007;18:308-13.
- Ritz T, Steptoe A et al. Emotions and stress increase respiratory resistance in asthma. *Psychosomatic Medicine* 2000;62:401-12.
- Weiner P, Massarwa F. The influence of gender on the perception of dyspnea in patient with mild-moderate asthma. *Harefuah* 2002;141:515-18.
- Tovhkorshynska MI, et al. Gender differences in psychological distress in adults with asthma. *Journal of Psychosomatic Research* 2001;51:629-37.
- Agrawal S. Effect of indoor pollution from biomass and solid fuel combustion on prevalence of self reported asthma among adult men and women in India: Findings from a nationwide large scale cross sectional survey. *J Asthma* 2012 Mar 7. [Epub ahead of print]
- Vignoud L et al. Smoking and asthma: disentangling their mutual influences using a longitudinal approach. *Respir Med* 2011;105(12):1805-14. Epub 2011 Aug 27.
- Sundberg R, Torek K et al. Asthma in men and women: Treatment adherence, anxiety, and quality of sleep. *Respir Med* 2010;104(3):337-44. Epub 2009 Nov 11.
- Chafin CC, Tolley E et al. Are there gender differences in the use of peak flow meters? *J Asthma* 2001;38:541-3.
- Goodman DE, Israel E et al. The influence of Age, Diagnosis, and Gender on Proper Use of Metered-Dose Inhalers. *Am J Respir Crit Care Med* 1994;150:1256-61.
- Ostrom NK. Women with asthma: a review of potential variables and preferred medical management. *Ann Allergy Asthma Immunol* 2006;96(5):655-65.
- Sell TH et al. Gender differences in the use of peak flow meters and their effect on peak expiratory flow. *Pharmacotherapy* 2005;25(4):526-30.
- Finch CK et al. Gender differences in peak flow meter use. *Nurse Pract* 2007;32(5):46-8.
- Clark NM et al. From the female perspective: Long-term effects on quality of life of a program for women with asthma. *Gen Med* 2010;7(2):125-36.
- Janevic, MR; Sanders G M; Thomas IJ et al. Study protocol for Women of Color and Asthma control: a randomized control trial of an asthma management intervention for African-American women. *BMC Public Health* 2012;12:76.
- Resta O, Carpagnano GE, Lacedonia D, Di Gioia G, Gilierti T, Stefano A, Bonfiro P. Gender difference in sleep profile of severely obese patients with obstructive sleep apnea (OSA). *Respir Med* 2005;99(1):91-6.
- Christine M. Lin, Terence M. Davidson and Sonia Ancohr Israel. Gender Differences in Obstructive Sleep Apnea and Treatment Implications. *Sleep Med Rev* 2008;12(6):481-96. doi:10.1016/j.smrv.2007.11.003.
- De Perrot M, Licker M, Bouchardy C, Usel M, Robert J, Spilopoulos A. Sex Differences in Presentation, Management, and Prognosis of Patients with Non-Small Cell Lung Carcinoma. *Journal of Thoracic Cardiovascular Surgery* 2000;119(1):21-6.
- Alexiou C, Onyeaka P, Beggs D, Akar R, Beggs I, Salama FD, Duffy JP, Morgan WE. Do women live longer following resection for carcinoma? *European Journal of Cardio-Thoracic Surgery* 2002;21:319-25.
- Ernster VL. Female Lung Cancer. *Annu Rev Public Health* 1996;17:97-114.
- Dresler C et al. Gender differences in genetic susceptibility for lung cancer. *Lung Cancer J* 2000;30(3):153-60.

Authors: Dr Antonio Infantino, Prof Amanda Barnard, Dr Irma Scarafino, Dr Ruben Infantino
Reviewer: Dr Barbara Yawn
Editor: Prof Mike Thomas

The views expressed in this sheet are not necessarily those of the IPCRG.
 Licensed under Creative Commons Attribution-No Derivative Works Licence. <http://creativecommons.org/licenses/by/nd/3.0/>
 The International Primary Care Respiratory Group (IPCRG) is a charity registered in Scotland working internationally (SC No: 035056) and a company limited by guarantee (Company number 256268)
 Date: April 2012 Author affiliations: for full list see www.theipcrgr.org