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**Title:** Absence of nonspecific bronchial responsiveness (NSBR) in occupational asthma (OA): A case-series study

Mr. Jacques André 5190 Pralong jacques-andre.pralong@hcuge.ch MD <sup>1</sup>, Mrs. Jocelyne 5191 L'Archevêque j-larcheveque@crhsc.rtss.qc.ca <sup>1</sup>, Mrs. Manon 5192 Labrecque manon.labrecque@umontreal.ca MD <sup>1</sup>, Mrs. Catherine 5193 Lemièrè catherine.lemiere@umontreal.ca MD <sup>1</sup> and Mr. André 5779 Cartier andre.cartier@umontreal.ca MD <sup>1</sup>. <sup>1</sup> Chest Medicine, Hôpital du Sacré-Coeur, Montréal, Canada .

**Body:** Background: Although increased NSBR is a key component of OA it may be absent in rare occasions as previously shown. Objective: Describe the prevalence of confirmed OA with normal NSBR before and after specific inhalation challenge (SIC). Methods: We retrospectively reviewed our database containing all SIC done in our laboratory or at work between 1997 and 2011. OA was defined by a positive SIC with a  $\geq 20\%$  sustained decrease in FEV<sub>1</sub>; normal NSBR was defined by PC<sub>20</sub>Methacholine (PC<sub>20</sub>M)  $> 16$  mg/ml. Results: 373/1193 workers tested had confirmed OA. 22/373 (5.9%) had normal NSBR before and after SIC. The mean $\pm$ SD delay between cessation of exposure at work and SIC was 96.2 $\pm$ 81.7 days. However, 10 subjects had at least one PC<sub>20</sub>M  $< 16$  mg/ml during their investigation while symptomatic and at work for 9 of them. The remainder 12 had normal NSBR on all tests but only 3 subjects had such a test while at work (2 while symptomatic). Among the 22 cases, 20 were atopic, 15 were exposed to a high molecular weight agent, 4 to a low molecular weight chemical and 3 to various agents during workplace challenge. Seventeen, 4 and 1 subjects had an early, late and atypical asthmatic reaction respectively. However, even if NSBR was always within the normal range, 3 subjects had a significant drop in PC<sub>20</sub>M ( $> 3.2$  fold) post-SIC and 13/14 showed an increase in sputum eosinophils count after SIC (mean increase of 9.9 $\pm$ 16.7%). Conclusions: We describe 22 cases of confirmed OA despite normal NSBR before and after SIC. This is however rare (5.9% of confirmed cases of OA by SIC). In our experience, it is exceptional to have normal NSBR while symptomatic and at work in cases of confirmed OA.