Refid	Author(s)	Title
18	Beretta C, Rifflart C, Evrard G, Jamart J, Thimpont J, Vandenplas O.	Assessment of eosinophilic airway inflammation as a contribution to the diagnosis of occupational asthma.
19	Engel J, van Kampen V, Gering V, Hagemeyer O, Brüning T, Raulf M, Merget R.	Non invasive tools beyond lung function before and after specific inhalation challenges for diagnosing occupational asthma.
20	Sastre J, Costa C, del Garcia Potro M, Aguado E, Mahillo I, Fernández-Nieto M.	Changes in exhaled nitric oxide after inhalation challenge with occupational agents
21	Lemière C, D'Alpaos V, Chaboillez S, César M, Wattiez M, Chiry S, Vandenplas O	Investigation of occupational asthma: sputum cell counts or exhaled nitric oxide?
22	Lemiere C, NGuyen S, Sava F, D'Alpaos V, Huaux F, Vandenplas O.	Occupational asthma phenotypes identified by increased fractional exhaled nitric oxide after exposure to causal agents
23	Moore VC, Anees W, Jaakkola MS, Burge CB, Robertson AS, Burge PS	Two variants of occupational asthma separable by exhaled breath nitric oxide level
24	van Kampen V, Brüning T, Merget R	Serial fractional exhaled nitric oxide measurements off and at work in the diagnosis of occupational asthma
25	Walters GI, Moore VC, McGrath EE, Burge S	Fractional exhaled nitric oxide in the interpretation of specific inhalational challenge tests for occupational asthma
26	Sastre J, Madero MF, Fernández-Nieto M, Sastre B, del Pozo V, Potro MG, Quirce S.	Airway response to chlorine inhalation (bleach) among cleaning workers with and without bronchial hyperresponsiveness
27	Vizcaya D, Mirabelli MC, Orriols R, Antó JM, Barreiro E, Burgos F, Arjona L, Gomez F, Zock JP	Functional and biological characteristics of asthma in cleaning workers

28	Mason P, Scarpa MC, Guarnieri G, Giordano G, Baraldi E, Maestrelli P	Exhaled nitric oxide dynamics in asthmatic reactions induced by diisocyanates
29	Ferrazzoni S, Scarpa MC, Guarnieri G, Corradi M, Mutti A, Maestrelli P	Exhaled nitric oxide and breath condensate ph in asthmatic reactions induced by isocyanates
30	13. Florentin A, Acouetey DS, Remen T, Penven E, Thaon I, Zmirou-Navier D, Paris C.	Exhaled nitric oxide and screening for occupational asthma in two at-risk sectors: bakery and hairdressing

Year of Publication	journal	Exposure/Occupation
2018	Allergy	HMW, LMW agents
2019	Int Arch Occup Environ Health.	HMW, LMW agents
2013	J Investig Allergol Clin Immunol.	HMW or LMW agents
2010	Chest	HMW & LMW agents
2014	J Allergy Clin Immunol	HMW & LMW agents
2010	Respir Med	HMW and LMW agents
2019	Am J Ind Med	HMW and LMW agents
2014	Lung	LMW
2011	Am J Ind Med	Sodium hypochlorite
2013	Respir Med	Cleaning products; mixture of domestic and occupational exposure

2016	Clin Exp Allergy	Isocyanates
2009	Chest	Isocyanates
2014	Int J Tuberc Lung Dis	Bakery and hairdressing

Comparator	Sample Size
SIC: FEV1 ≥20% from baseline (several challenges)	240: 133 SIC +/107 SIC-
Pulmonary responders to methacholine (FEV1 ≥20% & doubling of specific airways resistance (sRt) from baseline)/non responders SIC+: pulmonary responders AND/OR• ΔFeNO ≥ 13 ppb	122: 21 responders/101 non responders; 39 SIC+/83 SIC-
SIC+: ΔFEV_1 ≥20% from baseline	68 patients suspected to have occupational asthma, 45 of whom had a positive SIC
SIC: FEV_1 ≥20% from baseline	68: 26 positive SIC & 41 negative SIC (controls)
SIC: FEV1 ≥ 20% from baseline	178: 98 positive SIC
Methacholine airway hyperresponsiveness (MHC), PEF monitoring	60 patients confirmed with OA by PEF monitoring
SIC + (6)/ doubtful asthma monitored by FEV_1 and FeNO for 2 weeks of work exposure/2 weeks out of work	41 suspected and 6 confirmed OA
SIC: FEV_1 ≥ 20% from baseline	16 SIC +/ 16 SIC -
SIC: FEV_1 ≥ 20% from baseline	19: 13 cases OA to cleaning products/3 asthmatic controls/3 atopic subjects without hyperreactivity
Spirometry, HBR (11 cases/11 controls)	42 OA / 53 controls

SIC: FEV_1 ≥20% from baseline	26: 17 SIC+ /9 SIC -
SIC FEV_1 ≥20% from baseline + sputum eosinophils	39: 15 OA/24 controls
No comparator	178: 19 OA/159 controls

FeNO measurement	Adjustment
Baseline FeNO, cut off 25 ppb	Atopy, smoking
∆FeNO ≥13 ppb defined as difference between baseline FeNO and 24h after SIC	Atopy, smoking, treatment
Baseline & 24h after SIC	Atopy, smoking
Baseline, 7h and 24h after SIC	Atopy, smoking, treatment
Baseline and 24h after SIC	Atopy, smoking
Baseline FeNO before MHC and after PEF monitoring (cutt off for work-related increase: 14.7 ppb for smokers and 22.1 ppb for non smokers)	Smoking, atopy and inhaled corticosteroid
DFeNO; cut off for work related increase = 20 ppb	Smoking, atopy, treatement
Baseline FeNO and 24h from SIC; if baseline FeNO > 50 ppb the cut off for ∆FeNO set to > 20 %; if baseline FeNO < 50 ppb, the cut off for ⊗FeNO set to > 10%	Smoking, treatment
Baseline and 24h after SIC with bleach 0.4 ppm	Atopy, smoking
Baseline FENO	Atopy, smoking

FeNO monitored 7h after SIC and 24 after SIC;	Atopy, treatment
Baseline, 24h, 48 h and 7 days after SIC	
Baseline (occupationally exposed participants)	Smoking, atopy, steroid treatment

Findings
1. In SIC+, chances of high level of FeNO (≥25 ppb) are higher in atopic (OR: 2.9; 1.4-6.0; p=.004) and in never smokers (OR: 2.5; 1.2-5.0; p=.01). 2. HIstamine PC20 ≤16 mg/mL + FeNO levels ≥25 ppb and ≥50 ppb decreased the sensitivity (44% and 20%, respectively), and increased the specificity (78% and 94%, respectively) for a positive SIC result compared to HIstamine PC20 ≤16 alone (sensitivity 87% and specificty 36%). 3. Best sensitivity: Histamine PC20 ≤16 mg/mL OR sputum eosinophils ≥1% (94%), best specificity: Histamine PC20 ≤16 mg/mL AND FeNO ≥50 ppb
1. Increase in FeNO ≥ 13 ppb had a sensitivity of 0.57 and a specificity of 0.82 to detect the pulmonary responders. 2. If DFENO ≥ 13 ppb was included in the defintion of the SIC+ response, 18 of the pulmonary nonresponders became SIC+. 3. SIC + were younger (p = 0.04), with higher total IgE (p = 0.001), rate of atopy (p = 0.02), and specific allergen sensitization (p = 0.002) than SIC-. 4. SIC+ accounted for a possible false-negative classification of about 10% according to the expert overall evaluation of each individual case.
1.SIC+ showed an overall increase of 1.25 (95% CI, 1.05-1.48) 24 h postchallenge (p=0.01); no increase in patients with a SIC-. 2. In the separate analysis based on type of agent, only SIC with LMW agents induced a significant ΔFeNO 1.26 (P=.01). 3. For each unit increase in baseline FeNO, the probability of a positive SIC rises by 4%. 4. The cuttof in ΔFeNO = 41%provided a the best sensitivity (50%) and specificity (95%) of a positive SIC.
1. A ΔFeNO =10 ppb at 24 h postchallenge had a sensitivity of 36.8% and specificity of 81.2% for predicting a positive SIC. 2. A Δ in sputum eosinophil counts =2.2% achieved a higher sensitivity (78.9%) and similar specificity (81.2%) for predicting a positive SIC.
1. A post-challenge ΔFeNO ≥ 17.5 ppb had a specificity of 90% and a sensitivity of 45.3% for predicting a positive SIC. 2. The odds for a post-challenge ΔFeNO ≥ 17.5 ppb were significantly higher for HMW agents (OR: 4.2 [1.1-16.8], p=0.04).
1. Significant correlation between FeNO level and MHC, after controlling for confounders R2 = 0.221; p =0.009). 2. The area between curves (ABC) score based on mean PEF on work days and days away from work was not correlated to the DFeNO.
1. Serial FeNO measurements off and at work provide complementary information in the diagnosis in about one-fifth of cases with suspected OA, especially if specific inhalation challenges are negative or cannot be performed.
1. There was no significant difference between mean in ΔFeNO after positive SIC compared with control SIC, either in absolute ppb (p = 0.82) or in percentage of change (p = 0.85). 2. SIC + to LMW agents was associated with mean ΔFeNO of 7 % (95 % CI -15.73 to 29.6) or 2.1 ppb (95 % CI -6.07 to 10.19), not significantly different to controls.
1. Significant increase in mean ΔFeNO at 24 hr after bleach SIC (p=0.043).
1. Levels of FeNO similar in cases and controls.

1. FeNO increased after 24 h post SIC compared to exposure to sham ($p<0.05$) 2. Airways wall NO (JawNO) wass the fraction of NO responsible to the increase in FeNO after SIC.
1. Baseline FeNO significantly higher in SIC + (62 ppg vs 23 ppg) ($p<0.001$) 2. ∆FeNO significantly increases 24h and 48 h post-SIC 3. Prolonged FeNO increase (7 days after SIC) requests that SIC should be performed at a sufficient duration from the last exposure to isocyanates to avoid blunted response by an already elevated baseline FeNO 4. Baseline and 24-h FeNO positively correlated with the corresponding percentages of sputum eosinophils (baseline: 0.49, $p = 0.01$; 24 h: 0.71, $p =0.001$)
1.In a multiple linear regression model (height, case, smoking, corticosteroid treatment, total IgE), case/control status ($p=0.004$) and smoking status ($p=0.006$) were the only independent risk factors for the FeNO variation. 2. FeNO > 8.5 ppb was associated with the greatest sensitivity (78.9%) but had a low specificity (42.8%). 3. The combination of FeNO >8.5 ppb + positive questionnaire gave the best sensitivity (79%) and specificity (80.5%).