ALLERGIC RHINITIS IN THE EUROPEAN UNION

- Prevalence: 20-25%
- Population affected: >100 million
- Financial costs: 3.000 M €/year
  - Direct: 1,300 M
  - Indirect: 1,700 M

Bauchau V, Durham SR. Eur Respir J, 2004;24:758-64.
OCCUPATIONAL RHINITIS:
THE UGLY DUCKLING?
Table 1. Prevalence and etiological agents in occupational rhinitis

<table>
<thead>
<tr>
<th>Agents</th>
<th>Occupation</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High molecular weight agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory animals</td>
<td>Laboratory workers</td>
<td>6–33</td>
</tr>
<tr>
<td>Other animal-derived allergens</td>
<td>Swine confinement workers</td>
<td>8–23</td>
</tr>
<tr>
<td>Insects and mites</td>
<td>Laboratory workers, farm workers</td>
<td>2–60</td>
</tr>
<tr>
<td>Grain dust</td>
<td>Grain elevators</td>
<td>28–64</td>
</tr>
<tr>
<td>Flour</td>
<td>Bakers</td>
<td>18–29</td>
</tr>
<tr>
<td>Latex</td>
<td>Hospital workers, textile factory workers</td>
<td>9–20</td>
</tr>
<tr>
<td>Other plant allergens</td>
<td>Tobacco, carpet, hot pepper, tea, coffee, cocoa, dried fruit and saffron workers</td>
<td>5–36</td>
</tr>
<tr>
<td>Biological enzymes</td>
<td>Pharmaceutical and detergent industries workers</td>
<td>3–87</td>
</tr>
<tr>
<td>Fish and seafood proteins</td>
<td>Trout, prawn, shrimp, crab and clam workers; aquarists and fish-food factory workers</td>
<td>5–24</td>
</tr>
<tr>
<td><strong>Low molecular weight agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diisocyanates</td>
<td>Painters, urethane mould workers</td>
<td>36–42</td>
</tr>
<tr>
<td>Anhydrides</td>
<td>Epoxy resin production, chemical workers, electric condenser workers</td>
<td>10–48</td>
</tr>
<tr>
<td>Wood dust</td>
<td>Carpentry and furniture making workers</td>
<td>16–36</td>
</tr>
<tr>
<td>Metals (platinum)</td>
<td>Platinum refinery workers</td>
<td>43</td>
</tr>
<tr>
<td>Drugs (psyllium, spiramycin, piperacillin)</td>
<td>Health care and pharmaceutical workers</td>
<td>9–41</td>
</tr>
<tr>
<td>Chemicals</td>
<td>Reactive dye, synthetic fiber, cotton, persulphate, hairdressing, pulp and paper, shoe manufacturing workers</td>
<td>3–30</td>
</tr>
</tbody>
</table>
Prevalence and intensity of rhinoconjunctivitis in subjects with occupational asthma

- 40 patients with OA (mean time of exposure 10 yrs, with symptoms 5 yrs).
- Causative agents: HMW 24 subjects and LMW 14 subjects.
- Rhinitis symptoms 37/40 (92%), conjunctivitis 29/40 (72%)
- Prevalence of OR was similar for HMW and LMW agents, but intensity of symptoms was higher with HMW agents.
- Rhinitis preceded asthma (mean=22 months; 1 month-8 yrs)
  - 14/24 (58.3%) of HMW
  - 3/14 (21.4%) of LMW

OCCUPATIONAL RHINITIS & ASTHMA
Occupational asthma (OA) and occupational rhinitis (OR) are closely related and share etiological agents and mechanisms.

Symptoms of OR usually occur before symptoms of asthma.

OR has been considered an early marker of OA, particularly for high molecular weight agents.
ALLERGIC SYNDROME OF THE AIRWAYS
«UNITED AIRWAYS DISEASE»

Nasal cavity: allergic rhinitis

Bronchospasm
Inflammation
Prevalence of OR associated with OA, globally and according to the various causal agents; temporal relationships.

Data on incident cases of OA (2008-2010) were collected through the French national occupational disease surveillance and prevention network, using a standardised form including information on occupation, causal agents, presence of OR, and respective dates of OR and OA.

Among the 596 reported OA cases with latency period, 555 could be attributed to HMW agents (n=174) or LMW agents (n=381).

Overall, OR was associated with OA in 324 (58.4%) cases.

The frequency of association was significantly higher for HMW agents than for LMW agents (72.2% vs 51.5%, p<0.001).

OR occurred before OA significantly more frequently for HMW agents than for LMW agents (p<0.01).

Occupational rhinitis in workers investigated for occupational asthma

### Table 2
Outcome of specific inhalation challenge (SIC) based on nasal and bronchial response and type of suspected agent

<table>
<thead>
<tr>
<th>Group</th>
<th>Low nasal airway patency†</th>
<th>Low bronchial calibre*</th>
<th>RR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Total</td>
<td>Yes</td>
</tr>
<tr>
<td>Low</td>
<td>13</td>
<td>12</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>14</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>26</td>
<td>43</td>
<td>15</td>
</tr>
</tbody>
</table>

CI, confidence interval; HMW, high molecular weight; LMW, low molecular weight; RR, risk ratio.
*Clinically significant: decrease in FEV₁ ≥20% from baseline after challenge.
†Clinically significant: decrease in Vol₂−₅ ≥30% from baseline after challenge.
p Value by χ² and Fisher exact tests when appropriate.

Castano et al. Thorax 2009;64:50-4
Occupational rhinitis may be a predictor of occupational asthma severity

- 55 Italian and 17 Spanish subjects diagnosed with OA: 47 subjects had OA associated with OR (65%), 25 had OA without OR.
- LMW agents were more frequent in subjects with OA alone (p=0.06)
- Persistent asthma was more common in subjects with OA associated with OR (p=0.07).
- The time elapsed between the beginning of asthma symptoms and diagnosis tended to be shorter in subjects with OA and OR than in those with OA alone.
- **OA severity was associated with OR severity** (p<0.005).
- OR was a predictor of persistent OA (OR 4.1, 95% CI 1.2-14.6) after adjusting for causal agent, duration of asthma symptoms before diagnosis, bronchial challenge with methacholine, sex, age, smoking status, atopy and country.

Pala et al. (EAACI 2011, Abstract)
Position paper

Occupational rhinitis

The present document is the result of a consensus reached by a panel of experts from European and non-European countries on Occupational Rhinitis (OR), a disease of emerging relevance, which has received little attention in comparison to occupational asthma. The document covers the main items of OR including epidemiology, diagnosis, management, socio-economic impact, preventive strategies and medicolegal issues. An operational definition and classification of OR tailored to that of occupational asthma, as well as a diagnostic algorithm based on steps allowing different levels of diagnostic evidence, are proposed. The needs for future research are pointed out. Key messages are issued for each item.
Occupational rhinitis is an inflammatory disease of the nose, which is characterized by intermittent or persistent symptoms:
- nasal congestion
- sneezing
- rhinorrea
- itching

and/or variable nasal airflow limitation and/or hypersecretion due to causes and conditions attributable to a particular work environment and not to stimuli encountered outside the workplace.

OCCUPATIONAL RHINITIS: CLASSIFICATION

**Work-related asthma**
- Asthma caused by work = Occupational Asthma (OA)
  - Allergic OA (with latency period):
    - IgE-mediated
    - Non-IgE-mediated
  - Non-allergic OA (without latency):
    - Single exposure: RADS
    - Multiple exposures: Irritant-induced OA

**Work-related rhinitis**
- Asthma exacerbated by work = Work-Exacerbated Asthma (WEA)
  - Rhinitis caused by work = Occupational Rhinitis (OR)
    - Allergic OR (with latency period):
      - IgE-mediated
      - Non-IgE-mediated
    - Non-allergic OR (without latency):
      - Single exposure: RUDS
      - Multiple exposures: Irritant-induced OR
      - Corrosive rhinitis

WORK-RELATED RHINITIS

❖ **Occupational rhinitis**
  due to causes and conditions attributable to a particular work environment
  - Allergic (IgE-mediated or non-IgE-mediated)
  - Non-allergic (RUDS, irritant-induced)

❖ **Work-exacerbated rhinitis**
  - that is pre-existing or concurrent rhinitis exacerbated by workplace exposures

OCCUPATIONAL RHINITIS: DIAGNOSIS

Clinical and occupational history
Nasal examination

Immunological tests
(skin-prick tests or specific IgE antibodies)

Not available
(e.g. LMW agents)

Available
(e.g. HMW agents)

Negative
According to clinical history

Positive
According to required level of diagnostic confidence

Nasal provocation test in the laboratory

Positive

Negative

Not feasible

PROBABLE OCCUPATIONAL RHINITIS

Workplace assessment of:
Symptoms
Nasal patency
Nasal inflammation
Nonspecific hyperresponsiveness

DEFINITE OCCUPATIONAL RHINITIS

Positive

Negative

NON-OCCUPATIONAL RHINITIS

Onset of exposure

Immunologic sensitization
- IgE-mediated
- Non-IgE-mediated

[Contact urticaria]

Occupational rhinoconjunctivitis

Occupational asthma
Occupational rhinitis developing into occupational asthma

Rhinitis caused by ninhydrin develops into occupational asthma. P. Piirilä, T. Estlander, M. Hytönen, H. Keskinen, O. Tupasela, M. Tuppurainen

ABSTRACT: Ninhydrin (2,2-dihydroxy-1,3-indanedione or 1,2,3-triketo-hydridene hydrate) is a chemical used in the detection of free amino and carboxyl groups in proteins and peptides.

Allergic, immunoglobulin E (IgE)-mediated rhinitis caused by ninhydrin was diagnosed earlier in a 41 yr old woman working as a laboratory technician in a forensic laboratory. Despite handling ninhydrin only in a flow cabinet, symptoms of dyspnoea developed 6 months later. Peak flow was found to vary by 20% during working days. In the specific inhalation challenge it was shown that occupational asthma had also developed due to continuing slight exposure to ninhydrin. The titre of ninhydrin-specific IgE also increased from 0.6 to 1.1 kU·L⁻¹ in the follow-up.

This case stresses the importance of cessation of allergen exposure in occupational allergic rhinitis, in order to prevent asthma.


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ninhydrin
occupational asthma
occupational rhinitis

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Risk of Asthma Among Finnish Patients With Occupational Rhinitis*

Antti Karjalainen, MD; Rami Martikainen, MSc; Timo Klaauka, MD; Kimmo Saarinen, MD; and Jukka Uitti, MD

Study objectives: To determine the risk of asthma among patients with occupationally induced rhinitis. 

Design: Patients with confirmed occupational rhinitis were followed for asthma incidence through register linkage. Patients with other occupational diseases were used as a reference population. 

Subjects: Patients entered into the Finnish Register of Occupational Diseases in from 1988 to 1999 for occupational rhinitis (n = 3,637) or other occupational disease (n = 31,457) were observed until December 31, 2000, through two national registers of individuals who were eligible for the reimbursement of asthma medication and the Population Register Center. 

Methods: Incidence rates of asthma were calculated, and a log-linear model, adjusted for age, gender, and occupation, was used to estimate the relative risks (RRs) of asthma among those with occupational rhinitis compared to those with other occupational diseases. 

Results: There were 420 and 972 incident cases of asthma, respectively, among those with occupational rhinitis and the reference population. The crude RR of asthma was 4.8 (95% confidence interval [CI], 4.3 to 5.4) for all patients with occupational rhinitis, 5.4 (95% CI, 4.8 to 6.2) for those with occupational rhinitis accepted for compensation, and 3.7 (95% CI, 3.1 to 4.5) for patients with unaccepted occupational rhinitis. The RR varied according to occupation and was the highest among farmers and wood workers, both groups having a sevenfold risk. The risk was especially high during the year following notification, but a roughly threefold risk persisted several years thereafter. 

Conclusions: Patients with occupationally induced rhinitis have a high risk of asthma, but further studies are needed to establish the effect of preventive interventions.

(CHEST 2003; 123:283-288)
• Average duration of follow-up was 6-7 years
• Of the 3,637 patients with OR, 420 developed asthma (11.6%)
• Of the 31,457 control subjects, 972 developed asthma (3.1%)

The crude relative risk for asthma was **4.8%** (95% CI 4.8 to 6.2)

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Reference Population</th>
<th>Occupational Rhinitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Population</td>
<td>Cases of Asthma</td>
</tr>
<tr>
<td>Farmer</td>
<td>4,526</td>
<td>165 (3.7)</td>
</tr>
<tr>
<td>Animal husbandry worker</td>
<td>492</td>
<td>23 (5.3)</td>
</tr>
<tr>
<td>Textile worker</td>
<td>755</td>
<td>27 (3.6)</td>
</tr>
<tr>
<td>Electrical worker</td>
<td>1,576</td>
<td>51 (3.2)</td>
</tr>
<tr>
<td>Wood worker</td>
<td>1,964</td>
<td>36 (1.8)</td>
</tr>
<tr>
<td>Baker</td>
<td>299</td>
<td>13 (4.4)</td>
</tr>
<tr>
<td>Cook</td>
<td>518</td>
<td>20 (3.9)</td>
</tr>
<tr>
<td>Hairdresser</td>
<td>1,759</td>
<td>78 (4.4)</td>
</tr>
<tr>
<td>Cleaner</td>
<td>230</td>
<td>12 (5.2)</td>
</tr>
<tr>
<td>Other manufacturing or service worker</td>
<td>15,986</td>
<td>448 (2.8)</td>
</tr>
<tr>
<td>Other</td>
<td>3,412</td>
<td>99 (2.9)</td>
</tr>
</tbody>
</table>

*Values given as No. (%), unless otherwise indicated.

Hazard function estimates of asthma according to the time since the start of follow-up for the patients with occupational rhinitis and for the reference population.

Is this theoretical model satisfactory?

Sensitization to occupational allergens
Respiratory allergy in apprentice bakers: do occupational allergies follow the allergic march?

Background: This prospective study describes the incidence, risk factors and natural history of occupational respiratory allergy in apprentice bakers.

Methods: Two hundred and eighty-seven apprentice bakers were examined using a questionnaire, skin prick tests (SPTs) to common and occupational allergens, evaluation of total serum IgE level and specific anti-flour and α-amylase IgE, before, 1 year and 2 years after the onset of vocational training. To diagnose occupational respiratory disease, spirometry, histamine and allergen-specific inhalation challenge tests were performed.

Results: The incidence of work-related chest symptoms was 4.2% in the first year and 8.6% in the second year of exposure. Hypersensitivity to occupational allergens developed in 4.6 and 8.2% of subjects, respectively. The incidence of occupational allergic rhinitis was 8.4% after 1 year and 12.5% after 2 years, and that of occupational asthma/cough-variant asthma 6.1 and 8.7%, respectively. The latency period of work-related rhinitis symptoms was 11.6 ± 7.1 months and chest symptoms 12.9 ± 5.5 months. Only in 20% of occupational asthmatics could allergic rhinitis be diagnosed a stage earlier. In 21 out of 25 subjects with occupational asthma, chronic cough was the sole clinical manifestation of the disease. Stepwise logistic regression analysis revealed that positive SPT to common allergens was a significant risk factor of hypersensitivity to occupational allergens (OR = 10.6, 95% CI 5.27; 21.65), occupational rhinitis (OR = 3.9, 95% CI 1.71; 9.14) and occupational asthma (OR = 7.4, 95% CI 3.01; 18.04). Moreover, positive SPT to occupational allergens on entry to the training was a significant risk factor of asthma (OR = 6.9, 95% CI 0.93; 51.38).

Conclusions: The incidence of occupational asthma and rhinitis in apprentice bakers is high and increases with the duration of exposure. Skin reactivity to common and occupational allergens is the main risk factor of bakers' asthma. Most cases of work-related respiratory symptoms among apprentice bakers are related to a specific sensitization. In most subjects who developed occupational asthma, rhinitis occurred at the same time as the chest symptoms did.

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Key words: apprentices; asthma; bakers' incidence; natural history; risk factors.

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### Diagnosis of allergic respiratory diseases in apprentice bakers during the follow-up study (n = 287).

<table>
<thead>
<tr>
<th>Respiratory disease</th>
<th>Before</th>
<th>Developed during vocational training</th>
<th>Occupational</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At entry</td>
<td>1 yr</td>
<td>2 yr</td>
</tr>
<tr>
<td>Allergic respiratory disease</td>
<td>7 (2.4%)</td>
<td>16 (5.7%)</td>
<td>26 (9.8%)</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>6 (2.1%)*</td>
<td>15 (5.3%)</td>
<td>26 (9.8%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>0</td>
<td>9 (3.1%)</td>
<td>17 (6.1%)</td>
</tr>
<tr>
<td>Coexistence of allergic rhinitis and asthma</td>
<td>1 (0.4%)</td>
<td>8 (2.8%)</td>
<td>17 (6.1%)</td>
</tr>
<tr>
<td>Irritant effect on respiratory tract</td>
<td>–</td>
<td>8 (2.8%)*</td>
<td>2 (0.7%)*</td>
</tr>
</tbody>
</table>

* All of these subjects developed sensitization to occupational allergens and cough-variant asthma.
† Work related.

Dyspnea developed after 13.7 ± 6.6 months
Chronic cough developed after 13.6 ± 4.3 months
Rhinitis developed 13.5 ± 6.6 months
Rinoconjunctivitis preceded asthma only in 20% of cases (in most instances they developed simultaneously)
Most of the work related-related respiratory symptoms were associated to a specific sensitization
Occupational respiratory allergy was usually preceded by sensitization to common aeroallergens

OCCUPATIONAL RHINITIS: PROGNOSIS

Occupational rhinitis

Remission

Removal from exposure

Treatment

Persistent OR without OA

Ongoing exposure

Persistent OR with likely OA
SUMMARY & CONCLUSIONS

✓ OR is common among patients with OA.
✓ OR most often precedes the development of OA, especially when HMW agents are involved.
✓ OR is associated with an increased risk of asthma, although the proportion of subjects with OR who will develop OA remains uncertain.
✓ The “allergic march” is not always evident.
✓ Lack of standardized and validated diagnostic tools.
✓ The implementation of preventive measures for patients who have developed OR has not been systematically studied.
✓ Subjects with OR should be evaluated for OA.