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Occupational asthma in the salmon processing industry: a case series

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ABSTRACT

Objectives: Exposure to bioaerosols in salmon processing workers is associated with occupational asthma. IgE-mediated allergy and other disease mechanisms may be involved in airway inflammation and obstruction. Knowledge about disease burden, mechanisms, phenotypes, and occupational exposure is limited.

Methods: Salmon processing workers referred to our occupational medicine clinic from 2019-2024 were included in a patient register. They were investigated in line with current guidelines for management of occupational asthma, categorized according to diagnostic certainty, and characterized with focus on symptoms, work-tasks, and clinical findings.

Results: A total of 36 patients were included, among whom 27 had typical symptoms of work-related asthma, and 21 were diagnosed with occupational asthma. Among those with occupational asthma, all worked in the filleting or slaughtering area at the time of symptom onset. Median latency from start of exposure to symptom onset was 4 years. Fourteen (67%) of the patients with occupational asthma were sensitized to salmon. Three patients were sensitized to salmon skin but not salmon meat.

Conclusions: Occupational asthma among salmon processing workers displays a heterogenous clinical picture. IgE-mediated inhalation allergy towards various parts of the salmon seems to represent an important pathophysiological mechanism. However, some have occupational asthma with negative allergy tests. A comprehensive work-up strategy including early initiation of serial peak expiratory flow (PEF) and skin prick tests with various parts of the salmon should be considered. Although the incidence remains unknown, the substantial number of cases presented warrant increased efforts to reduce harmful exposure in the salmon processing industry.

What is already known on this topic

Salmon processing is associated with occupational asthma, and the main pathophysiological mechanism is suggested to be IgE-mediated allergy.

What this study adds

Salmon processing workers with occupational asthma could be sensitized to other parts of the salmon than the meat, and many have negative allergy tests. Spirometry based lung function tests have low sensitivity in detecting the disease.

How this study might affect research, practice or policy

We suggest a comprehensive work-up strategy with early initiation of serial PEF and skin-prick tests with different parts of the salmon. Further investigation of the predictive values of clinical tests, and updated knowledge about the occurrence of occupational asthma among salmon processing workers are needed.

INTRODUCTION

Exposure to bioaerosols containing fish proteins is associated with occupational asthma [1-3]. Two cross-sectional studies from the pilchard canning and fishmeal processing industry both showed a prevalence of occupational asthma of 2% [2, 4]. A cross-sectional study from a salmon processing plant found an 8% prevalence [1]. The three studies, however, used different definitions of occupational asthma, had heterogeneous exposures, and the design made them vulnerable to healthy worker bias [5]. Furthermore, the studies were performed several decades ago, with different production technology and facilities than today.

The main pathophysiological mechanism of occupational asthma associated with exposure to bioaerosols from fish is suggested to be IgE-mediated allergy [6]. The fish allergen parvalbumin (10-12 kDa) has been isolated from fish processing workplaces, and is in addition to other fish proteins proposed as a cause of occupational asthma among fish processing workers [6]. A case report from France described a salmon processing worker with occupational asthma who had specific IgE to salmon at 10.5 kU/L [7]. Another case report from Spain investigated two workers processing different fish species, who both had occupational asthma confirmed by specific inhalation challenge and were sensitized to the same fish species as they were processing [8]. Furthermore, a case-control study from Scotland described specific IgE as a predictor for occupational asthma among salmon processing workers [1].

The total number of workers employed in the Norwegian salmon and trout processing industry has increased by approximately 220% during 2003-2023, and amounted to 7322 workers in 2023. Salmon accounted for 95% of the production volume [9]. In the same period, occupational medicine clinics have experienced a marked increase in patients from the salmon industry referred with work related airway symptoms. This study presents a case series of occupational asthma in workers in the salmon industry. The aim is to describe symptom presentation, exposure scenarios and immunological findings in these patients, and indicate possible phenotypes and disease mechanisms.

METHODS

Subjects

All salmon processing workers visiting the occupational medicine clinic in St. Olavs Hospital, Trondheim University Hospital, Norway, from November 2019 to February 2024 were asked to participate in the study. The inclusion criteria were: 1) Working in the production area of a salmon processing plant, and 2) Presenting with respiratory symptoms. All but one of the patients were employed in one of three large facilities located along the coast of Central Norway, that currently employ approximately 1000 salmon processing workers altogether.

Procedures

The examining physician used a checklist with a questionnaire and health examinations in the patient workup. Some health examinations were done in all the patients, while others on indication only (Figure 1).

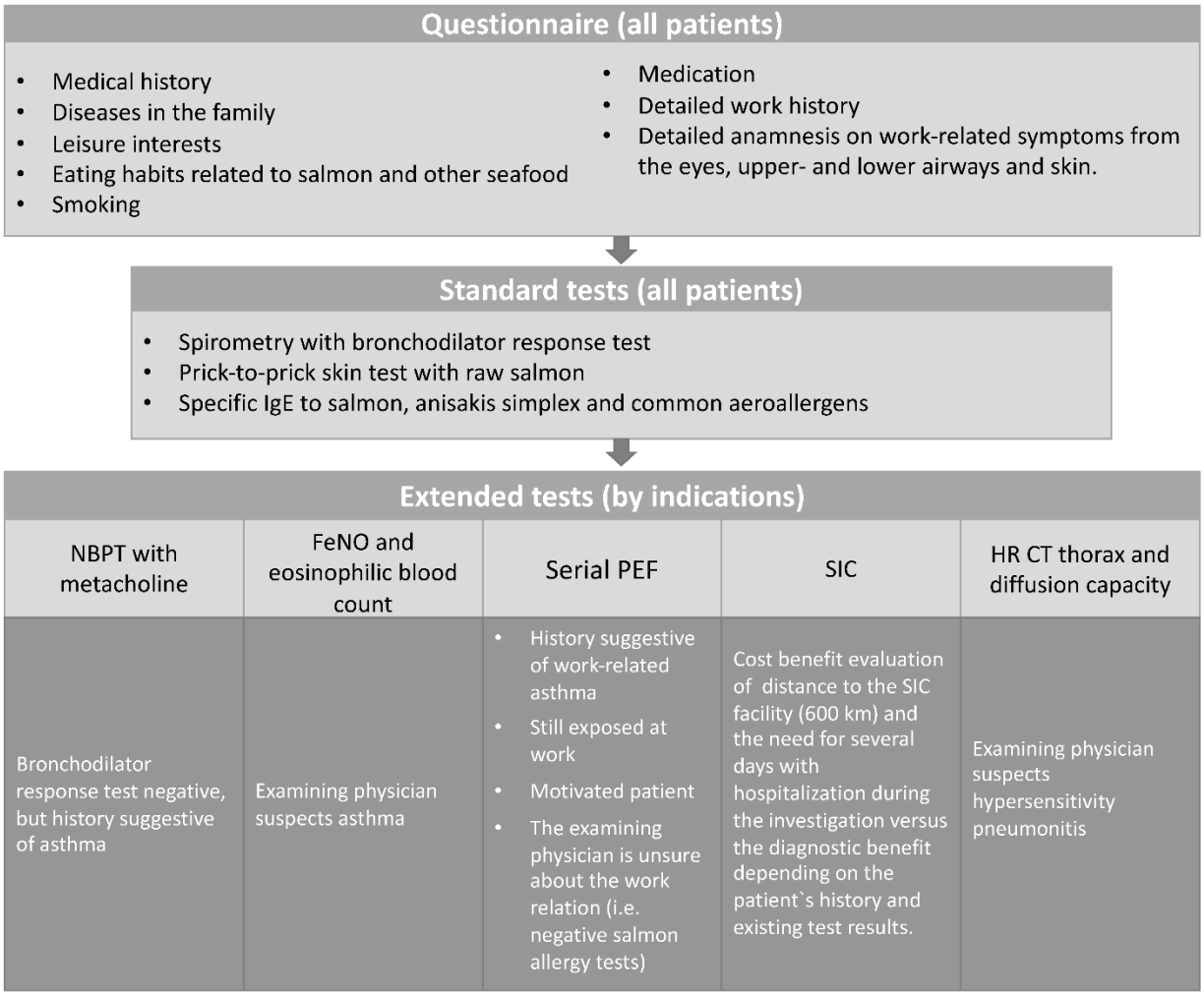

Figure 1: Procedure for the workup of respiratory disease among salmon processing workers. The questionnaire and lists of tests were part of an advisory checklist used by the examining physician. NBPT = Nonspecific bronchoprovocation test. Serial PEF = self-measurements of peak expiratory flow. FeNO = fractional exhaled nitric oxide. SIC = specific inhalation challenge.

Lung function tests

Spirometry with bronchodilator response test and nonspecific bronchoprovocation test with metacholine were done using a JAEGER Vyntus™ PNEUMO Spirometer (Vyaire Medical, U.S.) and performed as described in the ATS/ERS guidelines [10, 11]. If indicated, the workers were instructed to do self-measurements of peak expiratory flow (serial PEF) with an automatic logging Vitalograph asma-1 Asthma Monitor. They were instructed to perform the test approximately every two hours from the time they woke up until they went to bed over a period of approximately four weeks. Both periods at work and off work were included in the record. Mean diurnal variation and work-related pattern in serial PEF were assessed using the OASYS (Occupational Asthma SYStem) software [12].

Immunological tests and inflammatory markers

Serum analyses of total IgE, specific IgE to salmon and 12 common aeroallergens (Phadiatop™, TermoFisher Scientific, Uppsala, Sweden) were measured with fluoroenzyme immunoassay (ThermoFisher Scientific). Specific IgE analyses had a measurement range of 0.10-100 kU/L. Prick-to-prick skin tests (PTP ST) were performed with raw salmon meat, skin and viscera. The meat and skin were used without further processing. The viscera were homogenized using a domestic handheld blender prior to application. Each test was done at two test sites at least 2 cm apart at the patients' volar forearm using an ALK Spain single lancet (ALK-Abelló, Denmark). Soluprick™ positive and negative control (ALK-Abelló, Denmark) were used. In addition, five unexposed individuals were tested as negative controls (results shown in the supplementary table 2). Fractional exhaled nitric oxide (FeNO) was measured using Niox Vero (Circassia, Uppsala, Sweden), and blood eosinophil count using flow cytometry (Sysmex XN, Abbott Celldyn Sapphire, Siemens ADVIA 2120i). Specific inhalation challenge (SIC) was performed on selected patients at Haukeland University Hospital, Bergen, Norway, where twenty-five grams of raw salmon meat and twenty-five grams of salmon skin was homogenized, diluted in 200 ml water and aerosolized with a nebulizer, 30 centimetres from the patients` mouth in an exposure chamber.

Definitions

Work-related asthma symptoms were defined as breathlessness, wheezing, chest tightness or cough that got worse on workdays and better on weekends or holidays. If the symptoms first appeared prior to exposure to salmon bioaerosols, they were defined as work-exacerbated. If the symptoms first appeared after the patient started working with salmon, they were defined as symptoms of occupational asthma [13, 14]. Positive serial PEF was defined as an OASYS score >2.5. OASYS score is a work effect index, and a cut off on 2.5 has previously been shown to have a sensitivity of 75% and a specificity of at least 94% for the presence of occupational asthma compared to SIC, given optimal data [12, 15]. Positive SIC was defined as a fall in forced expiratory volume during the first second (FEV1) ≥15% from baseline [16]. A negative SIC was not considered valid if the test was carried out more than two years after the patient was exposed to salmon at work, as recommended by the National Norwegian Treatment Service for Specific Inhalation Challenge (Thomas Blix Grydeland, personal communication).

Excessive variability in lung function was defined as either positive bronchodilator response test, positive nonspecific bronchoprovocation test with metacholine, average diurnal PEF variability ≥10%, or largest FEV1-difference between visits >200 ml and ≥10% relative to the predicted value [17, 18]. Positive bronchodilator response test was defined as an increase in FEV1 of ≥10% relative to the predicted value, in accordance with the ATS/ERS guidelines [18]. Positive nonspecific bronchoprovocation test was defined as a fall in FEV1 from baseline of ≥20% after a cumulative provocative dose (PD20) with metacholine of <0.4 mg, as in accordance with the ATS/ERS guidelines [11]. Expiratory airflow limitation was defined as FEV1/FVC below lower limit of normal when applying the Global Lung Initiative (GLI)/Quanjer 2012 reference values [19]. Sensitization to salmon was defined as having a wheal diameter ≥ 3 mm larger than the negative control on the PTP ST and/or specific IgE against salmon ≥ 0.35 kU/L. Eosinophilic asthma was defined in accordance with the International Severe Asthma Registry (ISAR) Steering Committee, who defines the asthma as most likely eosinophilic if the blood eosinophil count at some time point is ≥ 300 cells/µl. The patient is also regarded as most likely eosinophilic if all of the following criteria is met: Highest registered blood eosinophilic count between 150-300 cells/µl, adult onset asthma and FeNO ≥ 25 ppb [20].

Data collection and identification of work-related asthma cases

Firstly, the examining physician recorded the tasks and symptoms as free-text in the patient`s medical journals. Secondly, the main author reviewed the medical journals of all the 36 included patients, and

extracted data on work tasks, symptoms and test results. The workflow in the salmon processing facilities consists of bleeding, gutting, de-heading, filleting, and packaging. Bleeding and gutting are carried out in the slaughtering area, while de-heading, filleting, and packing of fillets are carried out in the filleting area. Work tasks were either related to these processes or to cleaning of the production facilities. Further processing of salmon meat after filleting, like mincing, adding spice and smoking, is done at other factories/locations.

Recorded respiratory symptoms were described as fitting or not fitting to the definition of work-related asthma symptoms. If the symptoms were not work-related, or this was not clear from the journal text, the cases were excluded from the potential work-related asthma group. Cases were excluded if other diagnoses rather than asthma were considered the main cause of the respiratory symptoms. The remaining cases were considered as potential cases of work-related asthma. An expert panel of two specialists in occupational and pulmonary medicine reviewed these cases and categorized them into diagnostic groups based on experience and international guidelines [11, 14, 17, 18]. They thoroughly assessed the patients` history and clinical test results to conclude about the probability of work-related asthma in each case. A similar categorization has been done by Vandenplas et al [21], based on the work by Beach et al [22].

Ethics

All study participants signed a written consent in which they accepted the use of their medical record data in the present research project. The study was approved by the Regional Committee for Medical and Health Research Ethics in 2019 (case number 7158).

RESULTS

A total of 38 patients were asked to participate, among whom 36 agreed and were included in the study. Categorization of cases into diagnostic groups is shown in figure 2.

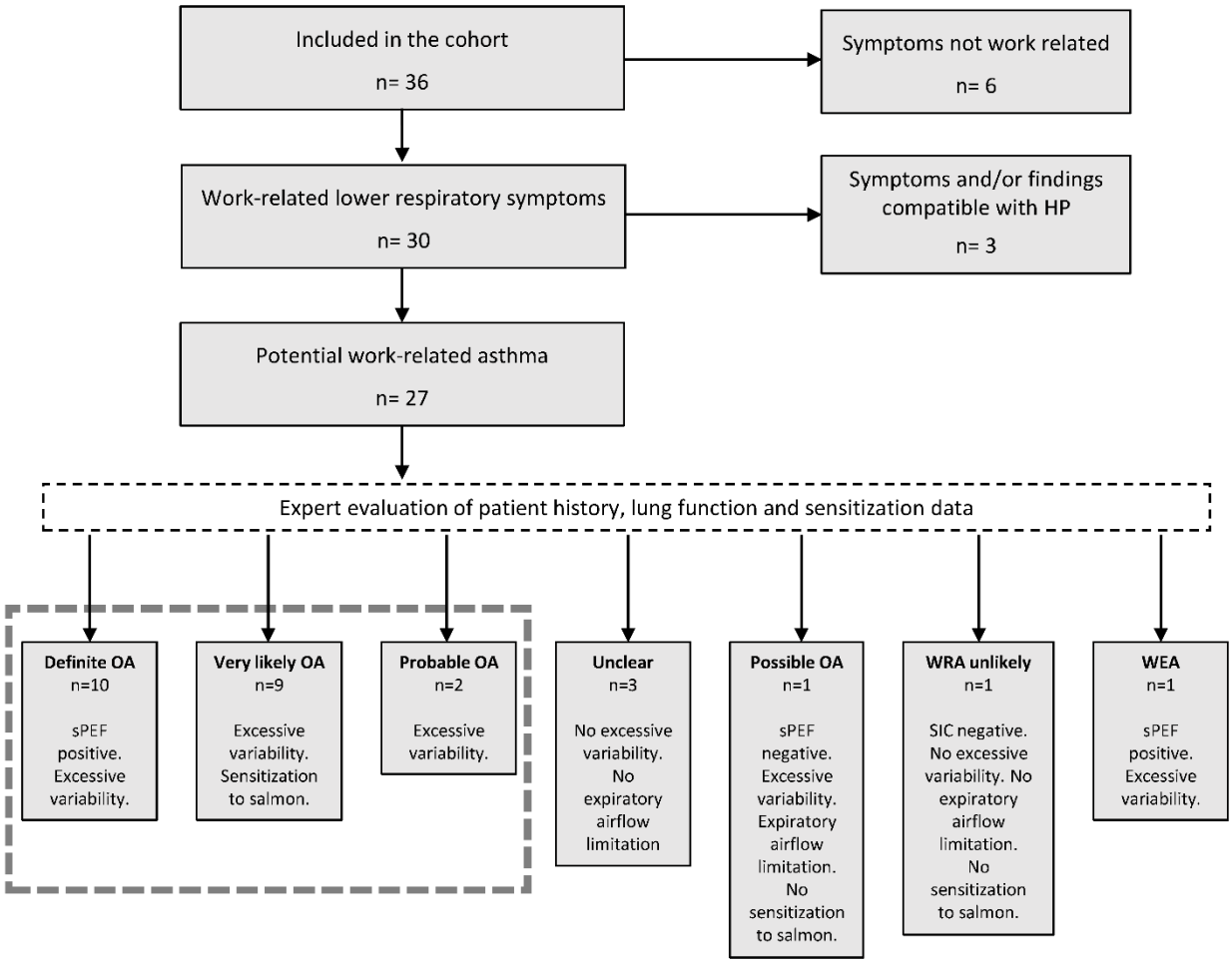

Figure 2: Categorization of cases. HP= hypersensitivity pneumonitis. WRA= work related asthma. WEA= work-exacerbated asthma. OA= occupational asthma. sPEF= serial measurements of peak expiratory flow. SIC= specific inhalation challenge. The grey dotted frame encircles the categories that together make up the category "occupational asthma" as presented in the text (n=21).

Potential work-related asthma cases (n=27)

Among the 36 patients included, 27 had typical symptoms of work-related asthma and were regarded as potential work-related asthma cases. All but one of them had more than one visit at the outpatient clinic. Among the 27 potential cases, 12 did serial PEF and 2 did SIC. Both SICs were negative, and one of them were considered not valid as it had been more than two years since last exposure. Hence, the expert clinicians made the diagnosis of occupational asthma predominantly based on the patient history, serial PEF measurements, sensitization to salmon and excessive variability in lung function. The expert evaluation resulted in seven diagnostic groups (Figure 2). In 3 out of 27 potential cases, the expert clinicians concluded differently than the examining physician, in the rest of the potential cases the conclusion was similar. Additional information including test results, symptom latency and work tasks among the 27 potential work-related asthma cases is given in the supplementary table 1.

Occupational asthma cases (n=21)

A total of 21 patients got a diagnosis of definite, very likely or probable occupational asthma after the expert evaluation (figure 1). Their patient characteristics are presented in table 1.

Table 1 Characteristics of the patients with occupational asthma (n=21)

Age (median, range)	33 (25-50)
Men n, %	15 (71)
Ethnic origin	
Eastern Europe	18 (85)
West Asia	2 (10)
Norway	1 (5)
Smoking n, %	
Nonsmoker	3 (14)
Current smoker	9 (43)
Ex smoker	9 (43)
Atopy* n, %	6 (29)
Prior lung disease n, %	
COPD	1 (5)
Childhood asthma	3 (14)
Years working with salmon processing (median, range)	7 (1-27)

* History of asthma, allergy or atopic dermatitis

Work tasks and changes in exposure

At the onset of symptoms, 10 out of the 21 cases worked with filleting, 5 with gutting, 3 with de-heading, 3 with bleeding, 3 with packing, 1 with cleaning, 1 with forklift driving, 1 with maintenance of the filleting machines, and 1 with fish quality check. Seven had more than one work task. All 21 worked in the slaughtering or filleting area of the processing plant, either full time or part time. At the first visit to the outpatient clinic, seven of the cases had either quit the job, or were on a sick leave due to work-related asthma symptoms. Fourteen (67%) had approximately the same work tasks as they had at the onset of symptoms. In February 2024, sixteen (76%) had quit their job or were on a sick leave, three (14%) were relocated to less exposed areas in the salmon processing plant and two had unchanged exposure. Twelve cases had changed the exposure from the first visit to February 2024 with a median time to cessation or reduction of exposure of four months.

Symptoms and sensitization to salmon

A total of 19 cases (90%) reported breathlessness, 12 (57%) cough, 11 (52%) wheezing, and 11 (52%) chest tightness that got worse on workdays and better at days off work. One reported redness and a warm feeling in the face, and one reported stomach pain after eating salmon. Two of the patients with occupational asthma were hospitalized due to work-related asthma attacks. One of them needed intensive care and was hospitalized for a total of 12 days. Sensitization to salmon was found in 14 (67%) of the cases. Three had a negative prick-to-prick skin test to salmon meat, but a positive reaction to salmon skin. Additional information about symptoms and test results among the 21 cases of occupational asthma are summarized in table 2.

Table 2. Salmon processing workers with occupational asthma diagnosed during 2019-2024

Case	Latency (mo)	Additional symptoms			Salmon sgE, kU/l	Total IgE, kU/l	Salmon PTP ST, mm				Phenotype	Verification of asthma		Serial PEF	Study diagnosis
		N	CU	IR			Positve/ negative control	Meat	Skin	Viscera		Excessive variability	Airflow limitation		
1	36	X			0.17	52	7.5/0	2.5	5.5	7.5	not eosinophilic	yes	no	positive	Definite OA
2	84	X			<0.10	297	3.5/0	4.5	3.8	NT	eosinophilic	yes	yes	positive*	Definite OA
3	96	X			<0.10	103	4.5/0	2.6	4.0	NT	not eosinophilic	yes	yes	positive	Definite OA
4*	96	X			<0.10	53	5.0/0	0	0	0	eosinophilic	yes	yes	positive	Definite OA
5	78	X			<0.10	146	4.0/0	2.0	0	0	eosinophilic	yes	yes	positive	Definite OA
6	30		X		0.14	64	6.0/0	3.0	3.5	4.8	eosinophilic	yes	no	positive	Definite OA
7	48				<0.10	NT	DM	0	0	NT	NT	yes	no	positive	Definite OA
8	48	X			<0.10	109	5.0/0	2.8	4.0	2.5	not eosinophilic	yes	yes	positive*	Definite OA
9	234				<0.10	78	NT	NT	NT	NT	eosinophilic	yes	no	positive	Definite OA
10	48				<0.10	18	4.5/0	0	NT	NT	not eosinophilic	yes	yes	positive*	Definite OA
11	4.5				0.41	57	NT	NT	NT	NT	eosinophilic	yes	yes	NT	Very likely OA
12	12				0.66	119	NT	NT	NT	NT	not eosinophilic	yes	yes	NT	Very likely OA
13	DM				5.30	610	7.3/0	7.3	6.5	7.0	eosinophilic	yes	yes	NT	Very likely OA
14*	48	X	X		1.25	>5000	4.5/0	4.0	4.0	4.3	eosinophilic	yes	yes	NT	Very likely OA
15	72	X			3.72	349	5.0/0	4.5	4.0	5.0	eosinophilic	yes	yes	NT	Very likely OA
16	72	X		X	12.80	331	6.0/0	6.3	5.8	5.3	eosinophilic	yes	yes	NT	Very likely OA
17	108	X	X		1.51	31	6.5/0	3.5	0	0	not eosinophilic	yes	yes	NT	Very likely OA
18	6			X	1.76	602	4.8/0	3.0	NT	NT	eosinophilic	yes	no	NT	Very likely OA
19	72				0.20	58	5.0/0	3.5	2.8	0	NT	yes	no	NT	Very likely OA
20	DM				<0.10	142	6.5/0	0	0	0	eosinophilic	yes	no	NT	Probable OA
21	3	X			<0.10	55	DM	0	0	0	eosinophilic	yes	yes	NT	Probable OA
Median	**48**				**0.14**	**106**									
Positive/cases studied		**11 /21**	**3 /21**	**2 /21**	**8/21**			**9/18**	**9/16**	**6/13**	**13/19**	**21/21**	**14/21**	**10/10**	

* Hospitalized due to severe occupational asthma. Latency = Months from start of exposure to salmon and debut of asthma symptoms. DM = Data missing. NT = Not tested. Additional symptoms= Other work-related symptoms in addition to the work-related asthma symptoms. N= Nasal symptoms; sneezing/runny nose. CU= Contact Urticaria after skin contact with salmon. IR= Symptoms of ingestion-related salmon allergy. sIgE= specific IgE. Positive test if sIgE >0.10 kU/l. PTP ST = Prick-to-prick skin test. Positive test if wheal diameter ≥3 mm. Eosinophilic phenotype = blood eosinophil count ≥ 0,3x10^9/L or ≥ 0,15 & < 0,3, adult onset asthma and FeNO ≥ 25. Excessive variability= One or more of the following: Positive bronchodilator response test, positive nonspecific bronchoprovocation test with metacholine, average diurnal PEF variability ≥10%, or largest FEV1-difference between visits ≥10% and 200 mL. Airflow limitation= FEV1/FVC below lower limit of normal when applying the GLI/Quanjer 2012 reference values. Positive serial PEF = OASYS score >2.5. *Suboptimal data for serial PEF interpreted by OASYS, but the serial PEF record is still interpreted as positive. The cases are sorted based on the probability for occupational asthma, and not time for inclusion.

DISCUSSION

The present study is, as far as we know, the largest case series of occupational asthma among salmon processing workers, and the first to report cases with occupational asthma and negative allergy tests in this industry. Our findings indicate that some salmon workers develop occupational asthma through non-IgE-mediated mechanisms. However, it is also possible that low test sensitivity may contribute to the substantial proportion of cases (33%) without confirmed salmon allergy. Nevertheless, most of the patients were sensitized to salmon, indicating that IgE-mediated allergy represents an important pathophysiological mechanism. Furthermore, most of them had eosinophilic asthma, a phenotype associated with type 2 inflammation and the production of IgE [20, 23]. The finding that some patients have positive prick-to-prick skin test to salmon skin while they are negative to meat, indicate that allergens in the skin or slime may cause occupational allergy and asthma. Thus, several pathophysiological mechanisms can be involved in the development of occupational asthma among salmon processing workers.

The symptoms presented by the patients in our study is similar to what has previously been described in case reports of occupational asthma caused by fish. A case report from Spain described one patient with dry cough and chest tightness that began one year after she started working in a fish freezing factory, and another patient with dyspnea, chest tightness and wheeze that began two years after he started working in a fish-smoking factory [8]. The latter patient had also work-related rhinoconjunctival symptoms and symptoms of ingestion-related fish allergy. Another case report from France described one patient presenting with rhinitis, dry cough and contact urticaria eight years after he started working at a salmon-processing plant [7]. Hence, there are indications that

occupational rhinitis, contact urticaria and ingestion-related fish allergy all are conditions related to occupational asthma caused by fish.

The three cases from Spain and France had a symptom latency ranging from one to eight years, which is within the range that we found in our study [7,8]. However, a cross-sectional study from Scotland described a substantial prevalence of occupational asthma among the workers only three months after the opening of a salmon processing factory, which could suggest a shorter latency [1]. Three of our cases reported a latency of less than a year, and one reported a latency of three months. We speculate that workers who develop symptoms quickly, tend to quit work without seeking medical care. Hence, short latency periods might be more common than what we see in our clinic, but we have no data on this. Prospective studies are needed to assess symptom latency in this industry.

The current study supports the evidence from previous studies that associate fish processing with the development of IgE-mediated occupational asthma [1, 7, 8]. A distinct form of food allergy, proposedly called Class 3 food allergy has been described among food processing workers in general [6]. In class 3 food allergy the primary sensitization route is inhalation, and reactions after ingestion of the same food are seldom [6]. In the present study, only two out of fourteen sensitized patients with occupational asthma did also have symptoms of ingestion-related food allergy to salmon. Hence, our findings are in concert with previous reports on IgE-mediated allergy caused by food processing.

Our findings supplement earlier studies of salmon processing workers that show a low or non-existing prevalence of sensitization to salmon [24, 25]. A survey of 46 salmon processing workers found no sensitization to salmon, although 9-15% of the workers reported work-related asthma symptoms such as wheezing, dyspnea and cough [24]. Another survey of 89 salmon processing workers showed a prevalence of sensitization to salmon of only 2% [25]. Both studies are cross-sectional epidemiologic studies, and therefore vulnerable to the healthy worker survivor bias, which could lead to an underestimation of sensitization and work-related asthma [5]. The present study, however, is limited to referred patients only, which could lead to a selection of more sensitized individuals. Furthermore, while we used both skin prick test and specific IgE to assess sensitization, these studies only used specific IgE. Thus, the difference in sensitization between these studies and our study, could be due to methodological differences.

Although previously reported asthma cases have elevated sIgE to salmon [7, 8], in-vitro studies suggest additional non-allergic mechanisms. In addition to known allergens such as parvalbumin, fish processing workers can also be exposed to bioaerosols containing detergents, disinfectants, endotoxins and other biological contaminants known to cause nonallergic inflammation [26]. One study found that rinsing water from a herring processing factory induced release of interleukin 8 and interleukin 1β from the blood cells of the herring processing workers [27]. Another study showed that the digestive enzyme trypsin from salmon can induce airway inflammation through interleukin 8-expression in cultured airway epithelial cells [28]. Thus, there is evidence to suggest that non-IgE-mediated immune responses could play a role in mediating inflammation in fish processing workers, as suggested by our findings.

This study emphasizes the importance of a comprehensive work-up strategy, as each test by itself showed low sensitivity in detecting occupational asthma. For example, 7 out 21 (33%) patients with occupational asthma had negative lung function tests at the first visit to the outpatient clinic, although most of them were still exposed to salmon, and had asthma symptoms in the weeks leading up to the test day (data shown in the supplementary table 1). Bronchodilator response test was positive in only 6 out 18 (33%) patients with occupational asthma, and nonspecific

bronchoprovocation test with metacholine (NBT) was positive in 10 out of 15 (67%). The relatively high proportion of negative NBTs could be because some of the patients were unexposed to salmon at the time the test was done, as the responsiveness to metacholine declines after cessation of exposure [29, 30]. Serial PEF require ongoing exposure at work. Hence, both serial PEF and nonspecific bronchoprovocation test with metacholine should be performed early in the work-up to increase the diagnostic certainty, as most of the patients went from being exposed to unexposed during the investigation. Consequently, in February 2024 we began to initiate serial PEF at first visit in all the study participants with work related asthma symptoms, regardless of other test results. This strategy is in line with the ERS guidelines, stating that "no measure of lung function or inflammatory marker is sufficiently sensitive to be used to exclude occupational asthma suggested by history" [14].

Furthermore, the allergy tests showed varying sensitivity in detecting sensitization, as some of the patients had positive prick-to-prick skin test to salmon but negative specific IgE. Although their predictive values are unknown in the setting of occupational asthma, this suggests that combining the prick-to-prick skin test with specific IgE increases the sensitivity in detecting allergy in this population. Our results also show that the combined test sensitivity increases when salmon skin and viscera are included in the prick-to-prick skin test, as some workers were sensitized to those tissues only. Hence, clinicians should consider including these tests when assessing sensitization in this population.

In the present case series, we describe a substantial number of occupational asthma cases among salmon processing workers in our region. In comparison, a total of 19 cases from the salmon and trout processing industry were reported throughout the UK in the period 1992-2017 [3]. Some workers develop severe lower airways disease, and one of the cases in our study were in the need of intensive care during an acute asthma attack. The problem is not limited to our region, as also physicians from other coastal regions of Norway are diagnosing salmon processing workers with occupational asthma [31] (Anje Höper, personal communication). This indicates that the current problem with occupational asthma may apply to the whole salmon processing industry. Recent scientific reports from other countries support this view [3, 7]. In the last four years, approximately five cases have been diagnosed at our clinic each year out of a total population of around 1000 workers. The true incidence, however, remains unknown. Nevertheless, the substantial number of cases in a small group underlines the need for increased efforts to reduce harmful exposures to salmon bioaerosols among salmon processing workers.

The study design makes the study vulnerable for selection bias. Referring doctors could emphasize sensitization status and therefore fail to refer patients with negative specific IgE to salmon. This may lead to an overestimation of the rate of sensitized salmon workers with occupational asthma. Another limitation is that 11 out of the 21 patients with occupational asthma were not examined with SIC or PEF, which makes the work-relation less certain. However, an otherwise comprehensive work-up and thorough expert evaluation, together with the fact that most of these patients were sensitized to salmon, partially remedies this limitation. A strength of the study is the substantial number of cases with detailed information on work tasks and symptoms. Another strength is the use of extended allergy testing with prick-to-prick skin test that included different tissues from the salmon, potentially increasing the sensitivity for salmon allergy. Still, the prick-to-prick skin test is not standardized and should therefore be interpreted with caution.

In conclusion, asthma among salmon processing workers displays a heterogenous clinical picture. The main mechanism is most likely IgE-mediated allergy, but non-IgE-mediated mechanisms may play a role in mediating occupational asthma among salmon processing workers. The patients can be

sensitized to various parts of the fish, and not only the salmon meat. Skin prick tests with various parts of the salmon may add valuable information in diagnosing allergic disease in this group of workers. Early initiation of serial PEF could be important for an objectively confirmation of work relation. There is a need for standardization and further investigation of the predictive values of skin-prick-tests with salmon meat, skin, and viscera. There is a need of updated knowledge about the prevalence and incidence of occupational asthma among salmon processing workers. Furthermore, there is a need for better characterization of the exposure levels to bioaerosols in different parts of the production line. Finally, we need studies that assess exposure-response correlations, to enable targeted advice about disease prevention in this emerging industry.

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Contributors CFF, HBL, AT, SS and SRS contributed to the design and planning of the study. CFF, LBR, HBL, AT, EH, SS, ABON and SRS contributed to the data collection. CFF contributed to the descriptive analyses. AT and SRS contributed to the expert evaluations of potential work-related asthma cases. CFF wrote and prepared the original draft. All authors (CFF, BEB, GT, HBL, AT, EH, SS, LBR, ABON and SRS) contributed to the manuscript, tables and figure preparation and have seen and agreed the final manuscript. CFF is responsible for the overall content as the guarantor.

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