OCCUPATIONAL ASTHMA IN SINGAPORE - A REVIEW OF CASES FROM 1983 TO 1990

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ABSTRACT

One of the newer occupational diseases in Singapore is occupational asthma. As on 31 December 1990 there were 35 confirmed cases of occupational asthma in the official statistics on occupational disease. We report in this paper our observations and experience based on these cases. The problem of under-reporting and the importance of early diagnosis are discussed.

Keywords: occupational asthma, diagnosis, causative agents

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INTRODUCTION

One of the newer occupational diseases in Singapore is occupational asthma. The first case in the official statistics on occupational diseases (Ministry of Labour) was confirmed in 1983. In recent years there has been an increase in the number of cases confirmed (Table I). If this trend continues, occupational asthma is likely to become an important occupational disease in Singapore in the 1990s.

By 31 December 1990 there were 35 cases of occupational asthma confirmed by the Ministry of Labour. We report in this paper our observations and experience based on these 35 cases.

MATERIALS AND METHODS

The 35 cases of occupational asthma arose from notifications to the Department of Industrial Health (DIH), Ministry of Labour and referrals to the Occupational Lung Disease Clinic, Tan Tock Seng Hospital (a clinic jointly run by specialist doctors from the DIH and Department of Medicine III, Tan Tock Seng Hospital).

Occupational asthma was defined as asthma that was due in whole or in part to agents encountered in the work environment. Evidence of asthma included one or more of the following: improvement in the forced expiratory volume in one second (FEV1) after bronchodilatation, documented asthmatic attack in a hospital or clinic, wheezing, presence of bronchial hyperreactivity (on histamine challenge testing) and a diurnal variation of 20% or more in the FEV1 or peak expiratory flow rate (PEFR).

Patients were interviewed for a detailed occupational history and a relationship of their symptoms to work. They were taught to use a Mini Wright's Peak Flow Meter and to record the readings on a form. Measurements were made every 3 hours throughout the waking hours. Each time three recordings were made and the highest of the three taken. The measurements were made over a period of about three weeks. This included a continuous period of about 7 - 10 days when they were away from their working environment eg home.

The daily maximum, mean and minimum PEFRs were plotted on a graph. Improvement of the PEFRs during periods away from the work environment and deterioration of the PEFRs during working periods were taken as evidence of work-related airway obstruction.

Visits were made to the workplace to identify possible causative agents. Environmental assessments were carried out to document exposure to suspected causative agents.

Where indicated, bronchial provocation tests to suspected causative agents were carried out on an in-patient basis. There were two main indications for bronchial provocation testing: (i) when there was more than one suspected causative agent in the work environment and (ii) when a new causative agent (not previously reported to cause occupational asthma) was suspected. Challenge testing to dusts was carried out by tipping the chemical from one tray to another. Challenge testing

Table I – Number of Occupational Asthma Cases Confirmed by Year

Year	No. of Cases
1983	1
84	2
85	0
86	4
87	3
88	7
89	7
90	11
Total	35

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to vapours was carried out by stirring or heating the liquid chemical.

Other investigations that were done included skin prick tests to common environmental allergens, chest X-ray examination, histamine inhalation testing and measurements of FEV1 and forced vital capacity (FVC).

RESULTS

Twenty-eight were males and seven were females. There were 22 Chinese, 10 Malays, two Indians and one Filipino. Their ages ranged from 18 to 65 years with a mean of 33.6 years (SD=10.5 years).

Causative Agents

Isocyanates

The most common causative agent was isocyanates accounting for 37% of cases (Table II). Four types of isocyanates were involved: toluene diisocyanate (TDI), diphenyl-methane diisocyanate (MDI), hexamethylene diisocyanate (HDI) and polyisocyanate. Eight of the cases (62%) were due to TDI. TDI is one of the chemicals used in the manufacture of polyurethane foam. Seven cases were working in factories making foam mattresses and cushions (Table III). Two cases were spray painters in engineering workshops. The paints used for coating trucks and boats contained HDI. Two cases were from the woodworking industry. They were spraying varnish containing isocyanates. One case was exposed to isocyanates used as an adhesive in the manufacture of fan belts. The remaining case was exposed to MDI which was used to make the insulation for refrigerators. Nine of these cases have been reported previously[1].

Table II – Occupational Asthma Cases by Causative Agent

Causative Agent	No. of Cases
Isocyanates	13
Soldering fumes	3
Welding fumes	3
Pharmaceutical drugs	3
Acid anhydrides	2
Ethylenediamine	1
Flour	1
Polyvinylchloride	1
Ozone	1
Coolant	1
Formaldehyde	1
Wood dust	1
Others	4
Total	35

Table III – Occupational Asthma Cases by Industry

Industry	No. of Cases
Polyurethane foam manufacture	7
Engineering/metal working	7
Electronics/electrical appliances	6
Pharmaceutical	4
Chemical	4
Woodworking/furniture	3
Plastic/rubber products	2
Others	2
Total	35

Other well established causes

There were three cases of asthma due to soldering fumes. They were all females working in the electronics industry where soldering is a common work process. The causative agent is probably the flux which is a substance used to clean the metal surfaces to ensure effective soldering. The flux may be incorporated in the solder wire (tin-lead alloy) or applied separately. There are different types of fluxes. Those containing colophony resin have been reported to cause asthma[2].

Welding is another common process in engineering or metal working factories. We had three cases of asthma due to welding fumes. Two were involved in manual metal arc welding and one in spot welding. Occupational asthma due to welding fumes has been briefly reviewed in our case report on asthma due to spot welding[3]. Welding fumes is a complex mixture of gases and particulates. Some of these are respiratory irritants (eg ozone, oxides of nitrogen, cadmium, zinc) or allergens (eg nickel, chromium or cobalt).

One worker developed occupational asthma from ampicillin after working for 13 years in a pharmaceutical factory. There were two cases due to acid anhydrides, a group of reactive chemicals used widely in alkyd and epoxy resins. One was a 34-year-old man who was exposed to both phthalate anhydride (PA) and maleic anhydride (MA) dust in the manufacture of alkyd and polyester resins. Both PA and MA have been reported to cause asthma[4]. What was interesting was that he had a negative challenge test to PA but reacted positively to MA, demonstrating the absence of cross-reactivity between the two anhydrides in his case[5]. There was one case of asthma due to ethylenediamine used in the manufacture of polyamide resins[6]. A baker in a biscuit factory developed asthma due to wheat flour[7]. There was one case of asthma due to formaldehyde which was used as a bonding agent in the manufacture of glass fibre pipes. One worker had occupational asthma due to ozone. He was exposed to ozone generated by electrical discharges during the charging of television tubes in the inspection section of a factory making television tubes[8]. A machinist developed occupational asthma from coolant mist. Asthma due to coolant mist has been recently reported[9].

New causes

Tylosin tartrate

Tylosin tartrate is a macrolide antibiotic used widely as an animal health and growth agent. Occupational contact dermatitis due to tylosin has been reported[10]. The first documented case of occupational asthma due to tylosin tartrate was a female laboratory technician from a small pharmaceutical factory in Singapore[11].

Polyvinylchloride (PVC) dust

Meatwrappers' asthma and asthma due to the thermal degradation products of PVC are well documented[12, 13]. Our case was the first reported case of asthma induced by occupational exposure to PVC resin dust at room temperature[14]. He was exposed to PVC dust in a factory manufacturing plastic seals for bottle caps. Workers exposed to PVC resin dust have been shown to have an increased diurnal variation in their peak expiratory flow rate[15].

Hexahydrophthalic anhydride (HHPA)

HHPA is an acid anhydride which has been suspected as a cause of asthma based on clinical histories and the demonstration of specific IgE[16]. Our case was the first case of HHPA induced asthma proven by a specific challenge test[17]. He was a laboratory technician in a factory producing epoxy-based coating chemicals.

Reaction time

A patient with occupational asthma when exposed to the relevant causative agent may develop an asthmatic reaction immediately (< 1 hour) or the reaction may be delayed (> 1 hour) or there may be a dual reaction (both immediate and delayed reactions).

In four cases the reaction time was not clearly established. Among the remaining 31 cases, 68% had a delayed reaction and 26% had an immediate reaction. In the case of asthma due to PVC dust his PEFR started falling only 9 hours after challenge to PVC dust[14]. In the case of asthma due to wheat flour, PEFR started falling only 7 hours after exposure to flour[7]. In both these cases there was no immediate reaction.

There were two cases where a dual or multiple reaction was documented. Both were due to acid anhydrides[5, 17].

Latent Period

The period between the onset of symptoms and first exposure or "latent period" ranged from two days to 13 years. Five cases (14.3%) had a latent period of less than one month. Sixteen cases (45.7%) had a latent period of one year or more. Six cases (17.1%) had a latent period of 10 years or more.

Bronchial hyperreactivity

Nineteen cases had the histamine inhalational challenge test done, of which 84.2% had evidence of bronchial hyperreactivity.

Atopy

Twenty-two cases had a skin prick test to common environmental allergens (Bencard test) done. 86.4% had positive reaction to at least one allergen suggesting atopy.

On the other hand, a personal history of atopy (childhood asthma, atopic dermatitis or allergic rhinitis) was obtained in only six out of 34 cases (17.6%).

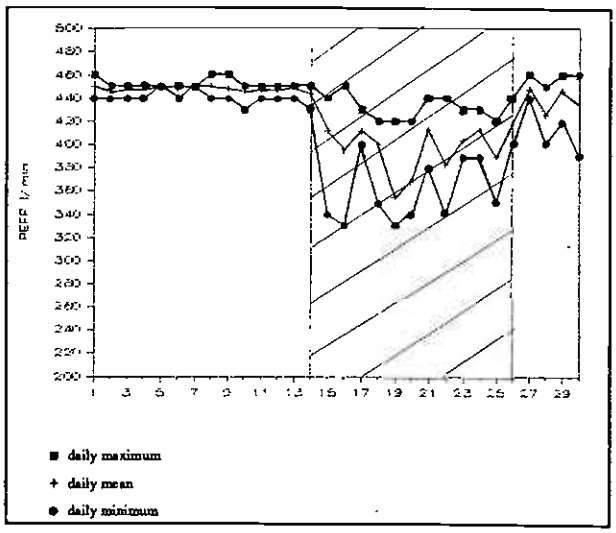
Smoking

Twenty-one out of 34 cases (61.8%) were never smokers. Seven (20.5%) were current smokers and six (17.6%) were ex-smokers. In one case (a male) we did not know his smoking status. All the seven females did not smoke. The prevalence of current smokers among the 27 males was 25.9%.

Serial PEFR records

Serial PEFR records showing improvement when away from work and deterioration at work were obtained in 22 cases. The PEFR records were plotted in a graph showing the daily maximum, mean and minimum PEFR. The graph of one of our cases due to soldering fumes is shown in Fig 1. There was firstly evidence of asthma, the maximum diurnal variation ex-

Fig 1 - Serial PEFR record of Mdm L who was exposed to soldering fumes in her working environment. Period at work is shaded. Periods at home are unshaded.

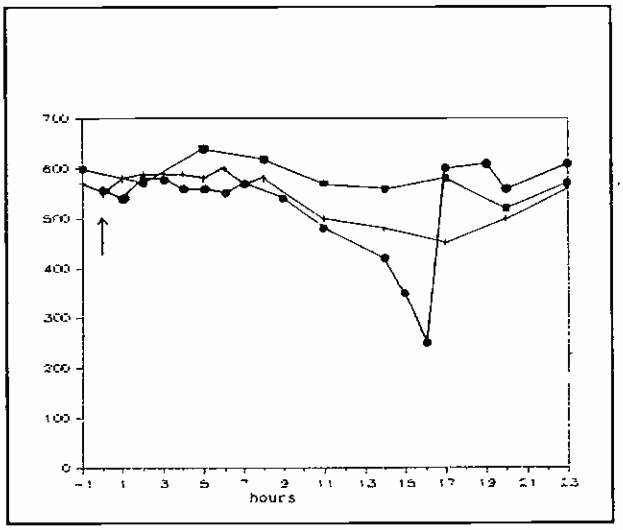


ceeded 20%. Secondly, the mean PEFR improved during weeks at home and deteriorated during weeks at work. There was also increased diurnal variation during weeks at work.

Bronchial provocation testing

Positive bronchial provocation tests were obtained in 10 cases. The chemicals used for provocation were in the form of dust (eg flour, PVC resin, tylosin tartrate, maleic anhydride) or volatile liquid (eg ethylenediamine, isocyanate, HHPA). In some cases the work process was simulated (eg soldering, painting or polyurethane foam making). PEFR was used to monitor for any asthmatic reaction. Exposure to the agent was for 20 minutes or less. Dust or vapour measurements were made to quantify the degree of exposure which was always kept below the threshold limit value of the chemical. In most cases, a baseline PEFR (for 24 hours) and/or a challenge to a control substance was also carried out before challenging to the test chemical. The results of the challenge test of the case due to unheated PVC resin dust is shown in Fig 2.

Fig 2 - PEFR baseline (■ day 1) and after exposure to lactose (+ day 2) and to PVC resin dust at room temperature (● day 3). Arrow indicates time of exposure on day 2 and 3.



DISCUSSION

Occupational asthma is probably grossly under-reported in Singapore. In Finland, in 1984 alone there were 179 reported cases of occupational asthma[18]. Finland's population of five million is only about twice that of Singapore. However the increasing number of cases confirmed in recent years reflects a growing awareness of the disease. Two developments may have contributed to this increase. Firstly, occupational asthma was made a notifiable and compensable industrial disease in September 1985. Secondly, the Occupational Lung Disease Clinic was set up in January 1988.

It is probable that the disease is under-reported because the occupational aetiology or relationship is easily overlooked. There are many reasons for this. Asthma is a fairly common condition. It has been estimated that two out of every 100 persons in industrialised countries have asthma and that 10% of these cases are work-related[19]. Thus, 90% of asthma cases are not work-related. There is a tendency to regard all cases of asthma as non-occupational.

Symptoms are often worse after work and at night, and may not even start while the patient is at work. Sixty-eight per cent of our cases had a delayed reaction. Several experienced symptoms more than six or seven hours after exposure. Hence the relationship of symptoms to the work may not be obvious even to the patient himself.

The latent interval between first exposure at work and the onset of symptoms may be rather long. Forty-six per cent of our cases had a latent period exceeding one year. Seventeen per cent had a latent period of 10 years or more. The mean latent period for colophony induced asthma was reported to be

four years and that for isocyanate asthma two years[20]. A common misconception is that the latent interval should be short.

Occupational asthma can induce non-specific bronchial hyperreactivity. Among those tested, 84% had evidence of bronchial hyperreactivity. Symptoms can develop not only at work but also with non-specific stimuli eg exercise, cold air and respiratory infections. The patient may have asthmatic attacks even when away from the work environment. And this makes the relationship to work less obvious.

Unfamiliarity with the causes of occupational asthma and the chemicals that are used in industry is another reason. The fact that an asthmatic patient works in a foam mattress factory may not mean anything unless the doctor is aware that isocyanates are used in the work process and that isocyanates can cause asthma.

It is both interesting and surprising that isocyanates was the most common causative agent among our cases. There are not many foam making factories in Singapore (less than 15) and the number of exposed workers is small (less than 100). We would have expected many more cases of occupational asthma from soldering fumes considering the large number of persons employed in the electronics industry, estimated at 129,000 in June 1988[21]. However, there were only 3 cases of asthma due to soldering fumes. Interestingly, isocyanates were also the most common causative agent for occupational asthma reported in 1989 in the United Kingdom[22]. It is not likely that a difference in the incidence rate of asthma between the various agents can account for this observation. A possible reason could be that isocyanate-induced asthma tends to be rather severe resulting in hospital admission. Nine out of 13 cases (69.2%) due to isocyanates were hospitalised for an asthmatic attack compared to five out of 22 cases (22.7%) for asthma due to other agents. In support of this could be the high levels of exposure to TDI in the foam making industry. Ninety-six per cent of 24 samples of air taken from 8 foam making factories exceeded the short term exposure limit of 0.02 ppm of TDI[23]. It is reasonable to expect a relatively higher degree of under-reporting of milder cases of occupational asthma, not requiring hospital admission.

It is also interesting that at least three new causes of occupational asthma were reported from Singapore. Lists of causative agents for occupational asthma may be long but not exhaustive. New chemicals are being introduced into industry all the time. We should be on the lookout for new causes of occupational asthma. For two of these agents, occupational contact dermatitis had earlier been reported (tylosin tartrate and HHPA). Agents known to cause allergic contract dermatitis may also cause allergic asthma if inhaled[24].

Finally, there is no simple laboratory test that can tell the doctor immediately whether the patient has occupational asthma or not. A single FEV1 and FVC is of little value in the diagnosis of occupational asthma[20]. Even with a pre-shift and post-shift FEV1, many cases of occupational asthma could be missed. The majority of our cases have been confirmed on the basis of serial PEFR records and/or bronchial provocation testing.

We have found the serial PEFR recording both a useful and practical diagnostic tool in the investigation of occupational asthma. It is based on many observations of the PEFR made over a prolonged period of time (weeks), both at home and at the workplace. Plotting the daily maximum and minimum PEFR in addition to the daily mean PEFR, enables us to evaluate not only the changes in the mean PEFR but also the diurnal variation. The PEFR recording requires the co-operation of the patient. Although some of our patients were not well-educated, all of them were given clear instructions on making the PEFR recording and we did not experience any significant problems with this.

Bronchial provocation testing was particularly useful in the documentation of new causes of occupational asthma or where the patient was exposed to more than one agent (eg the case which reacted positively to MA but not to PA). We also found it useful in cases where exposure to the suspected agent was intermittent (eg the case due to tylosin tartrate - she was exposed to this chemical only for one day per month).

Both atopy and smoking have been suggested as risk factors for occupational asthma[25]. Atopy appears to be a risk factor in asthma due to laboratory animal allergy[26] and platinum salt allergy[27]. So far no study of asthma caused by isocyanates[28], acid anhydrides or Western red cedar[29] have shown any strong association with atopy. Based on a positive reaction to at least one common environmental allergen on skin prick testing, 86.4% of the 22 cases tested may be considered atopic. This was not significantly higher than the 75.6% of 78 normal subjects who had positive skin prick test (not yet published). The prevalence of current smokers among the 27 males of 25.9% was comparable to the 25.3% in the male Singapore population in 1987[30].

Studies on the long term follow up of subjects with occupational asthma report a significant proportion (50% or more) who had left the workplace continued to have respiratory symptoms and bronchial hyperreactivity[25]. It has been suggested that the development of chronic symptomatic asthma seems particularly liable to occur in those with longer duration of symptomatic exposure[25]. Our cases are being followed up to study the outcome after removal from exposure.

Occupational asthma is not uncommon. It is important to consider the possibility of work-related asthma in a patient with asthma. Early diagnosis and removal from exposure could result in a better prognosis for the patient.

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