Recent trends in bagassosis in Japan

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Abstract

The only workers presently exposed to bagasse dust in Japan are the employees of sugar refineries and lacquerware factories. A follow up study of six former cases of bagassosis from among the retired employees of a paper board factory, closed since 1973, showed that none of the subjects still had bagassosis. Examinations of 70 employees of a sugar refinery for allergic reactions also showed no case of bagassosis. Seven cases with suspicious shadows of bagassosis on chest radiographs and four cases with positive serum precipitin to stored bagasse were, however, found among those 70 subjects. The results show the disappearance of a past episode of bagassosis and the possibility of a new occurrence of bagassosis among the employees of sugar refineries and lacquerware factories in the near future in Japan.

An outbreak of bagassosis among employees of a particle board factory in Okinawa Prefecture in the second half of the 1960s was the first occurrence of extrinsic allergic alveolitis in Japan.¹

This factory, the only one processing bagasse in Japan at that time, was closed in 1973 and since then no information on the prognosis of those subjects with bagassosis has been forthcoming, and no other occurrences of bagassosis have been reported. The sugar industry, from cultivation of sugar cane to its refinement, is still one of the most important regional industries in the rural districts of the south western part of Japan and produces bagasse. Recent sporadic reports of bagassosis from countries that had not reported that disease in the past²⁻⁴ indicate that it may

still be important to pay attention to the possibility of bagassosis in the world's sugar industry even today.

Therefore, studies about the actual state of bagassosis among the employees of the sugar industry and other industries handling mouldy bagasse should be made.

The purpose of the present study was to clarify the recent trend for bagassosis among workers engaged in occupations related to sugar refining and bagasse handling industries and to investigate the present condition of those patients who were diagnosed as having bagassosis at the last outbreak.

Materials and methods

RECENT SUGAR REFINING AND BAGASSE PROCESSING INDUSTRIES IN JAPAN

The actual state of exposure to bagasse and the work load of employees in the Japanese sugar refining and bagasse processing industry were analysed with data, collected from the Agricultural Policy Divisions and Agricultural Co-operative Associations of Kagoshima and Okinawa Prefectures and some private sugar refinery companies.

FOLLOW UP OF THE PAST CASES OF BAGASSOSIS

Among 24 men with bagassosis diagnosed by Naha Health Centre of Okinawa Prefecture in 1969-70 (the individual examination charts were provided by Professor Hokama, University of Ryukyus), six were still living in the south part of Okinawa Prefecture in the same area where the previous outbreak occurred. Four of the six cases agreed to examinations including a questionnaire on allergic conditions and job history, blood analysis, blood gas analysis, determinations of immunoglobulin concentrations, serum precipitin tests, lung function tests, chest radiography, and electrocardiography.

The original diagnoses had been made mainly on the basis of chest radiographs, respiratory complaints, and occupational history. Although the cases were not given sufficient examinations regarding allergy to make confirmed diagnoses of hypersensitivity pneumonitis, findings from the chest radiographs (fig 1 left) and clinical manifestations of the onset had indicated those cases to be typical bagassosis.

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Figure 1 Chest radiographs of Case A (56 year old man). Left: in 1969 with severe respiratory symptoms while working in the paper board factory (R-Chemical Co). Right: in 1989 working in D-sugar refinery without particular work related symptoms.

ALLERGIC CONDITIONS OF EMPLOYEES IN A SUGAR REFINERY

All 70 male employees, 54 factory and laboratory workers and 16 office workers of a D-sugar refinery in Okinawa Prefecture were examined for allergic conditions. Examinations consisted of questionnaires on allergic symptoms and grades of breathlessness described by Fletcher,⁵ histories of allergic diseases, job history, smoking habits, direct chest radiographs, determination of concentrations of serum immunoglobulins A, G, M, and E, serum precipitin tests to commercial moulds and bagasse extracts by double gel diffusion, and blood analysis.

Seventy male farmers growing mandarin oranges in Kagoshima Prefecture, located geographically close to Okinawa Prefecture, were selected as control subjects for the serum precipitin tests. The control subjects showed higher prevalence rates of skin symptoms, mainly developed by pesticide spraying, than the subjects of the D-sugar refinery, but there were no significant differences in mean ages and smoking habits between the two groups.

All of the subjects, including those of the follow up study, gave informed consent.

The extracts prepared for precipitin tests were bagasse (self made antigen), *S granarius*, *M faeni*, *T vulgaris*, *A fumigatus*, *C acremonium*, pigeon serum (from Hollister-Stier Co Ltd, USA), *Penicillium*, and *Alternaria* (from Torii Pharmacy, Japan). The procedures for preparing bagasse extracts and for the precipitin tests were as described by Pepys *et al.*⁶ Bagasse kindly given by the D-sugar refinery was collected from two places—namely, on the belt conveyer in a compressing area carrying bagasse immediately after it had been squeezed (immediate bagasse), and on the floor in a storing area (stored bagasse). Extracts from collected bagasse were prepared for the precipitin tests using Coca's solution and were partly cultured in Sabouraud broth (incubated at 25°C) and trypticase soy broth (at 52°C) for isolation and identification.

Results

SUGAR REFINING AND BAGASSE PROCESSING INDUSTRY IN JAPAN

The sugar refining industry in Japan is divided into three processes, cultivation and harvest of sugar

Figure 2 Flow sheet of sugar refining process.

cane, refinement of sugar, and processing of stored bagasse. The three processes are each managed by a different group of workers.

The sugar cane, accounting for 30% of the total yearly agricultural production in Okinawa Prefecture in 1987, is the most important agricultural crop in Okinawa Prefecture and 65% of the total sugar products in Japan (880 000 tonnes in 1987–8) came from Okinawa Prefecture and 35% from Kagoshima Prefecture. This, nevertheless, accounted for only 0.8% of the yearly sugar production in the world (data from Agricultural Cooperative Association Society of Okinawa Prefecture 1989).

The harvesting season, from December to April, overlaps the same season for sugar refining, so the farmers engaged in cultivation of sugar cane are not engaged in sugar refining at the same time: hence farmers are not exposed to bagasse dust.

The reaped sugar cane is carried to the regional

refining company and sugar juice is extracted by compressors four times in hot water and crystallised to sugar by heating. Most of the bagasse, after extracting the juice, is conveyed immediately and directly to the boiler room to be mixed with heavy oil and used as fuel for the heating process (fig 2). Over 95% of the bagasse is consumed for fuel in the sugar refining process and only 1–3%, 10–15 tonnes a year of the bagasse remaining after extraction, is conveyed to the storage room for processing into fertilisers, feed, materials for plant seed beds, etc. These processes are now in a tentative stage of being tested for commercial usefulness, so there are no workers continuously engaged in processes leading to high exposure to bagasse. These processes are carried out in a semi-closed system, except for bagasse conveying and bagging. Therefore, overall, airborne dust is not particularly dense throughout the refining process. The work rooms are rather dusty, however,

Figure 3 Bagging bagasse in the storehouse for forwarding to the lacquerware factory.

Table 1 Allergic examinations of case A and case B diagnosed with bagassosis after exposure at the particle board factory in 1969

	Case A	Case B
Age	56	57
Present occupation	D—sugar refinery	Occasional farmer
Past occupation	R—Chemical Co*	R—Chemical Co*
Duration of employment	1964–71	1964–9
Year of onset	May 1968	August 1970
Present complaints	Sneeze	Exertional dyspnoea
Present illness	NC†	Chronic bronchitis
Blood:		
Hb	14.2 g/dl	19.5 g/dl
Ht (%)	42.6	66.5
WBC	5800	8500
Eosinophils (%)	2	1
Pco ₂	Not measured	56.4%
Po ₂	Not measured	46.1%
IgE	61 U/ml	72 U/ml
IgA	256 mg/ml	281 mg/ml
IgG	1482 mg/ml	1675 mg/ml
IgM	54 mg/ml	131 mg/ml
Lung:		
% FEV ₁	89	42
% FVC	129	51
% V ₂₅	117	34
% V ₅₀	153	46
% V ₇₅	122	42
Chest radiograph	†	Overdistention, bulla, emphysema
ECG	Normal	Normal
Precipitin test‡	Negative	Negative

*Particle board factory.

†NC = Non-contributory.

‡Extracts: stored bagasse, immediate bagasse, commercial antigens from Hollister-Stier Co (*S granarius*, *M faeni*, *T vulgaris*, *Asp fumigatus*, *C acremonium*, pigeon serum).

from piled materials including pieced bagasse on the floor, wall, pillars, and frames in each workroom. Thus workers are exposed to some mouldy bagasse.

There are 34 sugar refineries in Japan, all using similar methods and handling an average of 1000 tonnes of sugar cane each day.

In the D-sugar refinery the stored bagasse is bagged (fig 3) and forwarded to lacquerware factories to be used as a replacement for traditional woods. This is the only work, except for the sugar refineries, in which workers are exposed to bagasse in Japan. There are 11 lacquerware factories in Okinawa Prefecture. All of these are minor enterprises with 10–20 employees. Although lacquerware manufacture may be considered to be more severe dusty work than that of sugar refining because of large amounts of stored bagasse in the process, it is difficult to clarify the exact number of employees and work conditions at those companies.

FOLLOW UP OF THE PAST CASES OF BAGASSOSIS

Table 1 shows the detailed data of the examinations for cases A and B among the six follow up cases.

Case A (56 years old) was an employee of the

particle board factory during 1966–70 and of the D-sugar refinery for the next 15 years. He has no serious complaints of respiratory symptoms and shows normal lung function tests at the present time, with complete recovery from abnormal shadows seen on the chest radiographs at the time of onset (fig 1). Case B (57 years old) was an employee of the particle board factory during 1966–71 and is a part time farmer at the present time. He still has symptoms consisting of severe exertional dyspnoea and periodically receives medical care for that condition. The present chest radiograph of case B (fig 4) showed overdistention of both lungs, emphysema and bulla of the upper lobes, but no fibrosis or rounded or irregular opacities. Mixed impairment of lung function and decline of Pco₂ and Po₂ were also found, indicating that the aetiology of his respiratory disorders was chronic obstructive respiratory impairment. Case C (58 years old) had worked for six years at the particle board factory and was a farmer. He had complaints of occasional cough and dyspnoea with a history of pneumonitis two years ago, without any finding of bagassosis on the present chest x ray film. Case D (48 years old) had worked 10 years at the factory, was

Figure 4 Chest radiograph of case B (57 year old man diagnosed as having bagassosis in 1969) in 1986 with severe attack of respiratory illness.

then an employee of a small ironwork factory, and was healthy, without any finding of bagassosis on the current chest x ray film.

No positive precipitin line to bagasse or other extracts was seen in any of the cases. Other examinations for allergies also showed no evidence of any remaining trace of past bagassosis in any of the follow up cases.

ALLERGIC CONDITIONS OF EMPLOYEES OF A SUGAR REFINERY

Table 2 shows the immunological and other clinical findings of the employees of the D-sugar refinery. Table 3 shows the results of the precipitin test to bagasse and fungal extracts. No significant differences were found between the factory and the office workers in the prevalence of abnormal findings of each current examination for allergies. There were seven (10%) subjects with abnormal findings such as diffuse linear shadows and small opacities on the chest x ray film (fig 5). Four (6%) subjects showed positive precipitin tests to bagasse extracts (fig 6), 14 (20%) subjects were positive to at least one of the test antigens. The precipitin lines were commonly more distinct to stored bagasse than to immediate bagasse.

By contrast, no subjects showed a positive reaction to bagasse extracts in the control group (table 3).

No close association of positive reactions to precipitin test with intensity of dyspnoea, chest x ray film, increased serum IgE concentration, and history of allergic diseases was seen among those subjects with positive precipitin to bagasse extracts (table 4).

Table 2 Rates of positive findings of allergic and other examinations for employees of D-sugar refinery

	No of subjects	Age	Years of employment	Allergy related symptoms*					Histories of AD†				Family histories of AD‡
				With	Re	Nose	Eyes	Skin	With	Re	Skin	Other	
Total	70	44 (10)	20 (6)	26	7	16	7	7	21	1	11	11	7
Factory	54	43 (10)	19 (10)	24	6	17	6	7	20	2	9	13	7
Office	16	49 (6)	21 (8)	31	13	13	13	6	25	0	19	6	6

	Increased serum immunoglobulins§				x ray film findings		Positive precipitin¶			Other examinations**						Smoking habit		
	E	A	G	M	Fib	Tbc	Bag	Fun	Other	WBC	CRP	Urine	Liver	BP	ECG	Curr	Ex	Non
Total	7	6	0	0	10	3	6	4	16	10	1	21	27	16	4	49	19	32
Factory	6	2	0	0	11	0	6	6	17	13	2	19	26	13	4	50	19	26
Office	13	19	0	0	6	13	6	0	13	0	0	31	31	25	4	44	19	38

*Complaints of symptoms associated with work: Re = Respiratory (cough, phlegm, short of breath, etc).

†Allergic diseases: asthma, bagassosis, nasal allergy, conjunctivitis, contact dermatitis, and collagen disease.

‡Relatives with allergic diseases within the second degree.

§+ 700 U/ml for IgE; + 400 mg/ml for IgA; + 1800 mg/ml for IgG; + 300 mg/ml for IgM.

||Fib = nodular or reticular pattern shadow, or diffuse interstitial fibrosis, or both; Tbc = tuberculosis.

¶Bag = extracts of stored or immediate bagasse; Fun = commercial extracts by Hollister-Stier's kit; Other = self made antigens of *C. albicans* etc.

**8000/ml for WBC, increase in C-reactive protein, increase in at least one among glucose, protein urobilinogen, and occult blood in urine, + 35 KU for GPT, or + 40 KU for GOT, or 60 U/l for r-GTP. + 150 mm Hg for systolic blood pressure or + 90 mm Hg for diastolic blood pressure. Abnormal findings of ST and T on electrocardiography.

Table 3 Results of precipitin tests to bagasse and other fungi extracts for employees of D-sugar refinery and farmers

	Employees of D-sugar refinery* No (%)	Farmers* No (%)
No	70	70
Age (mean (SD))	44 (9)	48 (10)
Allergic symptoms:		
Respiratory	5 (7)	5 (7)
Nose	11 (16)	2 (3)
Eyes	5 (7)	7 (10)
Skin	5 (7)	21 (30)
One or more	18 (26)	26 (37)
Allergic history	15 (21)	13 (19)
Allergic family history	5 (7)	7 (10)
Smoking habit:		
Current	34 (49)	33 (46)
Ex	13 (19)	8 (11)
Never	23 (32)	31 (41)
Positive precipitin:		
Stored bagasse	4 (6)	0 (0)
Immediate bagasse	2 (3)	0 (0)
<i>S granarius</i>	0 (0)	0 (0)
<i>M jaeni</i>	1 (1)	0 (0)
<i>T vulgaris</i>	1 (1)	0 (0)
<i>Asp fumigatus</i>	0 (0)	0 (0)
<i>C acremonium</i>	0 (0)	0 (0)
<i>C corticale</i>	0 (0)	0 (0)
<i>Pigeon serum</i>	0 (0)	0 (0)
<i>Pigeon droppings</i>	0 (0)	0 (0)
<i>C albicans</i> †	9 (13)	17 (24)
<i>Fusarium</i> ‡	2 (3)	1 (1)
One or more	14 (20)	17 (24)

*Only male subjects.

†Self made antigen from IFO 1060 kindly provided by Professor M Tokunaga, Kagoshima University.

‡Self made antigen from isolated fungus collected in the working environment of a cattle raising barn.

As also shown in table 4, one subject out of four with positive precipitin tests and two subjects out of seven with abnormal chest radiographs were office workers. Only one subject out of four with positive precipitin tests and all of the subjects with abnormal findings on x ray film were smokers or ex-smokers with high values for the Blinkman index.

Penicillium, *Fusarium*, and *Rhizopus* were identified on the mould separating culture and also some unidentified thermophilic fungi were isolated from the tripticase soy broth. Detailed data on those fungi will be reported elsewhere.

Discussion

Bagassosis is extrinsic allergic alveolitis caused by occupational inhalation of bagasse dust during bagasse processing in the manufacture of papers, building materials, fertilisers, feed, and refractory bricks, etc.⁷ Since the first report by Jamison and Hopkins,⁸ occurrence of bagassosis has been reported all over the world, especially in countries with a large

scale sugar industry.⁹⁻¹³ The scale of the Japanese sugar industry is small compared with other countries, although it has a long history. Therefore, the amount of bagasse is not large, and specific processes involving the handling of bagasse are not regarded as posing serious health hazards. In fact there was no bagasse processing factory in Japan until 1964 when the episodic particle board company was opened. No case of bagassosis had been reported before then.

According to the report of Tsugu,¹ the first case of bagassosis occurred two months after the opening of the board factory that used bagasse and urea resin adhesives as main materials. Ten cases out of 134 employees were diagnosed with bagassosis during November 1966 and October 1967. Those subjects, in whom the symptoms developed after a latent period of 2-24 months, mainly complained of shortness of breath, cough, and general dullness and showed miliary tuberculosis-like shadows on their chest radiographs. Although no other immunological examinations were taken for those cases, the diagnosis of bagassosis was considered to be reasonable

Figure 5 Fibrotic finding on the chest radiograph of an employee of the sugar refinery (subject 7, table 4) without precipitin to bagasse extract and respiratory symptoms at work.

Figure 6 Positive reaction of precipitin test to bagasse extract (subject 4, table 4). Distinct precipitin to extract of stored bagasse (2) and also weak precipitin to immediate bagasse (1) are shown.

because of their clinical manifestations and the association with bagasse handling works. *A flavatus*, *Rhizopus*, *Trichoderma*, *Candida*, *Penicillium* and other kinds of fungi were identified. Subsequent to that report, another 24 employees were diagnosed as having bagassosis by their clinical symptoms and chest radiographs after examination at the Naha-Health Centre.

Later, Abo¹⁴ confirmed that a higher proportion of those employees had precipitin antibody to the bagasse extract and that bagasse extract gave

precipitin lines with serum from animals sensitised to *A niger*. These findings indicate that there is no doubt about the diagnosis of bagassosis from sensitisation to mouldy bagasse in employees of the board factory. Since the factory closed, there have been no investigations of and no reports on bagassosis in Japan.

From the follow up study on six former cases of bagassosis, it was confirmed that no case (including one case (case A) exposed presently to bagasse) remained with obvious evidence of bagassosis continuing since the time of onset in the 1960s, leading to the conclusion that the first episode of bagassosis has left no cases in Japan.

The sugar industry is still operating, however, as one of the important regional industries in rural districts in Japan. Moreover, as above, there are still sporadic reports on bagassosis from various areas in the world from which little information has been available until now.^{2,4} There is also a new publication on criteria for the diagnosis of bagassosis.¹⁵

As shown from the results, workers exposed to bagasse dust are restricted to the employees of sugar refineries and lacquerware factories at the present time in Japan. Therefore we selected the employees of a D-sugar refinery as the subjects for the present study.

The results indicate that bagassosis did not occur among the employees of the sugar refinery. Some cases, however, showed abnormal shadows on their chest radiographs, suspected to be hypersensitivity pneumonitis, and positive reactions to precipitin tests to bagasse extracts. Those findings and conditions are not, of course always associated with active hypersensitivity pneumonitis. On the other hand, there were no subjects showing positive precipitin tests to bagasse extracts among the control subjects, indicating that an antigenic agent specific to the

Table 4 Individual data from the allergic examinations showing positive precipitin to bagasse extract or fibrotic findings on chest radiograph

No	Age	Sex	Years of employment	Precipitin*			Chest radiograph†	Shortness of breath by HJ‡	Symptoms at work§							History of AD	Smoking habit¶	Place of job
				B	H	O			C	F	W	N	E	F	D			
1	29	M	6	+	-	-	-	I	-	-	-	-	-	-	-	Ur, CD	Smoker (150)	Laboratory
2	49	M	27	+	-	-	-	I	-	-	-	-	-	-	-	Rh	Ex (15)	Factory
3	50	M	30	+	-	+	-	I	-	-	-	-	-	-	-	-	Never	Factory
4	48	M	27	+	-	+	-	I	-	-	-	-	-	-	-	Ur, CD	Never	Office
5	41	M	13	-	-	-	+	I	-	-	-	-	-	-	-	-	Smoker (340)	Factory
6	27	M	4	-	-	-	+	I	+	-	-	-	-	-	-	-	Smoker (80)	Factory
7	48	M	27	-	-	-	+	II	-	-	-	-	-	-	-	-	Smoker (840)	Factory
8	58	M	11	-	-	+	+	I	-	-	-	-	-	-	-	-	Ex (720)	Office
9	51	M	23	-	-	-	+	I	-	-	-	-	-	-	-	-	Ex (400)	Office
10	49	M	25	-	-	-	+	I	-	-	-	-	-	-	-	-	Smoker (360)	Factory
11	38	M	12	-	-	-	+	I	+	-	-	-	-	-	-	-	Smoker (400)	Factory

*B = bagasse extracts; H = Hollister-Stier's kit. O = *C albicans* (self made).
†Nodular or reticular pattern shadow or diffuse interstitial fibrosis, or both.
‡The grade of shortness of breath by Hugh-Johns' criterion.
§Always complain when at work. C = cough; P = phlegm; W = wheeze; N = nasal symptoms; E = symptoms of eyes and conjunctiva; F = fever; D = dullness.
||AD = allergic diseases; Rh = rhinitis; Ur = urticaria; CD = contact dermatitis.
¶Blinkman index in parentheses.

bagasse handling workers might exist in the bagasse extracts.

These findings suggest that the employees of sugar refineries might be sensitised by inhalation of bagasse dust originating from mouldy piled materials in the work room and that clinical cases of bagassosis might develop if the workers were exposed to large amounts of mouldy bagasse. Although the aetiological agent could not be confirmed by our present study, we identified some fungi, considered to be antigenic, from the working places. Since the first report of Pepys *et al.*,¹⁶ some kinds of fungi have been recognised, in general, as the causative antigens for bagassosis, especially *Thermoactinomyces vulgaris* and *sacchari*.^{17,18} From the results of the current precipitin tests, we found no evidence for an association between those two kinds of fungi and the precipitin antibody among the positive subjects.

At the present time preventive control measures for bagassosis in other parts of the world seem to consist of various ways of improving the storing process.¹⁹ These control measures should be introduced into the bagasse processing factories in Japan. Such measures are, however, more appropriate to large scale industries, and would be difficult to adopt in small scale factories like those in the Japanese sugar industry.

The results indicated that there may be workers with bagassosis in present day Japan, even though the first episode of bagassosis has disappeared, and further investigations should be carried out to detect any such cases among workers with bagasse, especially those engaged in lacquerware companies. The working conditions during the bagasse handling process should also be improved in a manner suitable to the actual conditions in each workplace.

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