BAKER'S ASTHMA (GRAIN-DUST-INDUCED ASTHMA)

by C.S. Ted Tse and P.K. Raghuprasad

ASTHMA can be caused by occupational exposure to various dusts, vapors, and fumes. The term *grain-dust-induced asthma* is used to indicate asthma caused by exposure to grain dust. The definition encompasses a variety of airway disorders that may result from an immunological mechanism. Although baker's asthma is the more familiar subset and is caused by an occupational exposure to grain dust in bakeries, millers, farm workers handling grain, and those employed in docks may also develop asthma.[1-3] In addition, outbreaks of asthma occurring in people exposed to grain dust carried by wind from neighboring mills have been described.[3] The prevalence of baker's asthma has ranged from 2.1 percent to 30-50 percent in different series.[4] The following is a case report of a patient with baker's asthma.

CASE REPORT

A 48-year-old black male was well until December 1977 when he had an onset of wheezing, dyspnea on exertion, and cough productive of whitish sputum. He complained of increasing attacks of wheezing and coughing for two months, starting about five hours after he had been at work. He had worked as a baker, making pies, since 1968. The attacks of wheezing were usually preceded by sneezing and rhinorrhea, which lasted about 30 to 60 minutes. These attacks were also usually accompanied by coughing and sweating, but fever and chills had not been documented. He had no family or personal history of allergies, eczema, asthma, or hay fever. He smoked three to four cigarettes per day until May 1978, when he stopped smoking. He had been seen at a local emergency room on several occasions for acute asthma attacks. Oral aminophylline, prescribed by the emergency room physician, had afforded some relief. The patient was referred for further allergy evaluation.

Initial physical examination revealed a well-developed, well-nourished black male in no acute distress. Vital signs were normal, and there was no evidence of rhinitis or bronchial asthma. Routine laboratory results were as follows: complete blood count—hemoglobin 12.9 g/dL, hematocrit 39.8%, white blood cells 10 000/mm^3; differential — neutrophils 44%, lymphocytes 39%, basophils 1%, monocytes 13%. Chest X-ray was normal. Skin prick tests for sensitivity to common aeroallergens were performed by standard methods[5] and were negative except against *Alternaria* and *Hormodendrum* (both 4+) and dust (3+). Commercial wheat extract elicited a 3+ reaction, but other cereal extracts elicited no reaction. Total IgE, measured by paper radio-immunosorbent test (PRIST), was 200 U/ml (400 ng/ml); normal is 5-250 U/ml. Specific IgE, measured by radioallergosorbent test (RAST), showed low binding against the common allergens ragweed, timothy, box elder, and cat and dog danders. RAST was not performed against the cereals. Serum precipitins were negative.

Pulmonary function was assessed by measuring forced expiratory volume in one second (FEV_1) before and after the bronchial provocation test (Figure 1). Exposure of the patient to nebulized extracts of commercial wheat extract showed no evidence of bronchial constriction (decrease in FEV_1 was insignificant). Repeated bronchial provocation tests, performed by the method described by Pepys and Hutchcroft[6] and using wheat flour from the bakery in which the patient worked, showed strong positive reaction. In this method, the subject shakes 250 g of the suspected flour from one tray to another for a period of 30 minutes in an enclosed environment.[6] Baseline readings of FEV_1 are taken during the hour preceding the exposure and at ten-minute intervals during the half hour of exposure. Thereafter, hourly readings are recorded until late evening. A drop in $FEV_1 > 20$ percent is considered a positive provocation. In this patient, FEV_1 dropped from 1.8 L at time zero to 0.7 L in ten minutes (61 percent decrease). It was considered unnecessary to proceed with further confirmatory tests, such as the leukocyte histamine release, in view of this violent reaction to the bronchial provocation test.

The diagnosis of wheat-grain-induced asthma was

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confirmed. Further bronchial challenge tests using various potential contaminants were scheduled, but the patient was lost to follow-up.

Clinical Manifestation

The earliest recorded case of grain-dust-induced disease was reported by Ramazzini, who, in 1713, observed dyspnea and urticaria caused by grains and grain dusts.[7] A comprehensive study was undertaken in 1964 by Williams et al., who analyzed, by questionnaire, a vast population of workers at grain elevators in Saskatchewan, Canada.[8] Of a total of 502 grain elevator agents, half (54 percent) had a history of one or more of the following symptoms related to grain dust: cough, wheezing, breathlessness, grain fever, or dermatitis. Breathlessness was encountered in 15.5 percent of the subjects, and this was directly related to both advancing age and length of service. Grain fever, with symptoms of chills, fever, shivering, and muscle ache, was observed in 6.1 percent of the subjects. The other clinical manifestations were dermatitis (13.9 percent), irritation of the eyes (46 percent), and irritation of the nose (23 percent).

Clinical Course

In a recent study conducted by Popa and co-workers to determine the relationship of length of occupational exposure, sex, and age to the occurrence of baker's asthma, it was found that rhinitis and bronchitis appeared after 9 years of working, while bronchial asthma occurred after 14 years, and that rhinitis always preceded asthma. The mean age of onset of respiratory symptoms was 40 years. Rhinitis and bronchitis began at an earlier age (34.1 years) than asthma (43 years). All subjects were 33 years or older at the onset of their allergic symptoms. Rhinitis with or without bronchitis occurred more frequently in females than in males.[9]

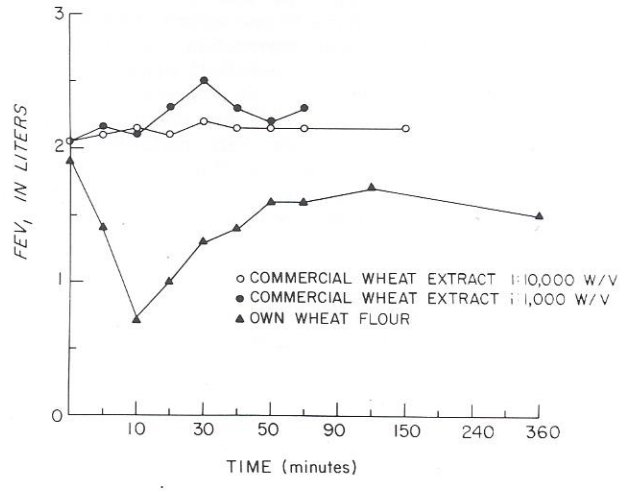

Figure 1. Bronchial provocation test in patient with grain-dust-induced asthma. Commercial wheat extract elicited no response; patient's own bakery wheat flour resulted in immediate positive response.

Table 1. Possible Etiological Agents in Grain-Dust-Induced Asthma

CEREAL GRAIN FLOURS
Barley
Corn
Oats
Rye
Wheat: albumin, globulin, gliadin-4 fractions, gluten and glutenin
CONTAMINANTS
Fungi: parasitic (smut or rust) saprophytic (*Aspergillus, Alternaria*)
Chemicals: fumigants, pesticides
Mites: e.g., *Glycophagus granarius*
Insects, animal parts, excreta
Bacterial endotoxins, fungal metabolites: e.g., aflatoxin

Pathogenesis of Grain-Dust-Induced Asthma

Since baker's asthma is the most-studied in this group of disorders, it will be given particular emphasis in this discussion. Although grain-dust-induced asthma was described centuries ago, limited information was presented to explain its pathogenesis. Inhalation of cereal dust has been suggested as the primary cause of the disease.[10] Earlier surveys of grain elevator agents found that smokers had an increased incidence of cough and sputum production compared with nonsmokers.[9] This would indicate that both cigarette smoking and exposure to grain dust might result in bronchial mucosal hyperplasia and bronchitis. Particles smaller than 5 μ have been found to be important in causing chronic lung diseases, presumably due to their penetrating ability.[11,12] However, in the pathogenesis of asthma due to true sensitivity to grain dust, the size of the particles is not considered important. Rather, the various antigens contained in the grain dust are more likely to be important. Grain dust contains a mixture of organic materials such as fungal spores; insect, rodent, and bird parts; and excreta, in addition to the cereals. Any of these is a potential asthmogen (Table 1).

Stresemann reported immediate asthmatic reactions in flour workers following inhalation tests with nebulized extracts of flour and/or arthropod contaminants,[13] whereas Hendrick and others documented two cases of baker's asthma with dual asthmatic reaction to bronchial provocation with flour.[14] The respiratory symptoms that developed after exposure to grain dust were either immediate wheezing or chest tightness of a slower onset, which became worse after several hours. Immediate hypersensitivity skin test response to the extract of crude grain dust and aqueous extracts of flour were reported in subjects exposed to and having respiratory symptoms.[14-16] Wilbur and Ward reported comprehensive immunological studies in a case of baker's asthma. They demonstrated immediate skin hypersensitivity and positive histamine release to wheat extract, passive transfer skin tests,

and successful blockage of such transfer by heat inactivation and specific anti-IgE immunoadsorption. Furthermore, provocation using the patient's bakery wheat extract reproduced immediate bronchial response.[17] These studies convincingly suggest an IgE-mediated type I hypersensitivity.

Other immunological mechanisms have been reported also. Activation of the alternative complement pathway by ground whole rye and airborne dust was reported by Olenchock et al.[18] Immediate reactive intradermal tests to either *Alternaria* or *Aspergillus* antigen in two cases of baker's asthma were reported by Klaustermeyer et al. Bronchial provocation tests with *Aspergillus* revealed a dual asthmatic response, and an immediate response was shown to *Alternaria*.[19] These airborne fungi may have contributed to the pathogenesis of other cases of baker's asthma. Baldo and Wrigley demonstrated specific IgE antibodies (as measured by RAST) to many components of wheat flour in sera of two patients with baker's asthma. The strongest reactions were observed with wheat albumin and globulins.[20] The mechanism underlying the late asthmatic reaction is controversial; a type III Arthus-like response, thought to be characteristic of allergic alveolitis, has been suggested,[14] but IgE-mediated late cutaneous and bronchial reactions are being recognized increasingly.[21]

Diagnosis

Crucial to diagnosing baker's asthma is knowing the patient's occupational history and the temporal relationship of the patient to exposure at work. An important clue to the possibility of the disease being work-related is the abrupt onset of asthma in an adult with no previous history of allergic disease. The symptoms of asthma tend to develop after exposure at work and improve during weekends or vacations. Chest examination may be normal, and chest X-ray is usually normal. Physical examination of the worker, in the office, may not be helpful, but examination at work, during exposure, may lead to diagnosis.

Certain laboratory tests are helpful in diagnosing baker's asthma (Table 2[5,22-24]). Bronchial provocation testing, using the "occupational-type exposure," is the most specific procedure in documenting asthmatic response to suspected allergens. Like the asthmatic reaction following exposures at work, immediate, late, or dual asthmatic reaction to the provocation test may occur.

The patient presented here demonstrated many features peculiar to baker's asthma: for instance, the long period of sensitization before the symptoms of asthma appeared, absence of fever and chills, normal chest X-ray, specificity of bronchial provocation tests, and complexities in establishing the nature of the specific asthmogen. Some of these features helped us to distinguish this entity from hypersensitivity pneumonitis.[25]

The patient showed skin test reactions to some aeroallergens and to wheat extract. Bronchial chal-

Table 2. Diagnostic Aids in Grain-Dust-Induced Asthma[5,22-24]

LABORATORY TEST	CRITERIA	CLINICAL SIGNIFICANCE AND EXPLANATION OF TEST
Total blood eosinophils	> 400/mm^3	Elevated eosinophils in peripheral blood may occur in atopic allergy and parasitic infections. Eosinophils preferentially phagocytize IgE-containing immune complexes.[22]
Total IgE (PRIST)	> 250 U/ml	This test quantitates the amount of total IgE in human serum. IgE is significantly elevated in most patients with allergic diseases, such as extrinsic asthma. It may be a rough guide in distinguishing between allergic and nonallergic asthma.
Specific IgE (RAST)	> 10% binding	This test measures the amount of allergen specific IgE in serum and correlates well with clinical allergy in patients sensitive to pollens, epidermals, and some foods.[23]
Skin tests	> 2+ (read in 10 to 20 minutes)	The immediate skin test reaction is a result of the interaction between specific antigen and IgE skin sensitizing antibodies bound to mast cells, which causes the release of histamine and other pharmacologic mediators. It is useful in diagnosing extrinsic asthma and allergic rhinitis. If skin tests are negative or equivocal, the RAST and bronchial provocation tests should be employed to confirm diagnosis. In skin tests (prick method), 1+ = erythema only; 2+ = 1-2 mm wheal; 3+ = 3-4 mm wheal; 4+ = wheal > 4 mm with pseudopodia.[5]
Leukocyte histamine release	≥ 50%	The peripheral blood leukocytes of an allergic individual liberate histamine in the presence of specific antigens. In the diagnosis of allergies, a high correlation between histamine release and skin test response was found.[24]
Bronchial provocation	≥ 20% ↓ in FEV_1 or 25% ↓ in FEF_{25-75}	This test is the most accurate method of corroborating suspected natural and occupational allergens. It is also used as a standard with which to compare other tests, such as RAST or skin tests. FEF_{25-75} measures small airway obstruction.

↓ = decrease, FEF_{25-75} = forced expiratory flow between the 25th and 75th percentile of the forced vital capacity

lenge with commercial wheat extract elicited no response, but the patient's own wheat flour, when used for provocation, resulted in immediate asthmatic response. This may mean that the patient's asthma was in response to one or more antigens contained in his bakery flour (e.g., molds or insect parts; see Table 1), but absent from the commercial wheat extract. Further bronchial challenge tests, using various potential contaminants, might have established a more specific etiologic diagnosis in this case, but the patient did not report for further procedures.

Treatment

The best therapeutic approach to the management of baker's asthma is the avoidance of future exposure to the allergen. Often, the symptomatic patient has to be removed from work because even a low concentration of the allergen can provoke an asthmatic attack, and continued exposure can lead to irreversible airway obstruction.[26] However, this may not be practical, and the use of special masks or respirators is often recommended. These masks may not be effective and often are not worn because of discomfort.

The pharmacologic treatment of baker's asthma does not necessarily differ from that of other types of asthma. Isolated or intermittent episodes of mild asthma should be treated initially with drugs having β-adrenergic activity (e.g., aerosol sympathomimetic agents such as albuterol, isoproterenol, or metaproterenol). Theophylline derivatives (aminophylline, theophylline, and oxtriphylline) or the selective β_2-stimulating agents (terbutaline, albuterol) may help diminish symptoms of baker's asthma.[26]

Parenteral therapy may be required to abort acute bronchospastic episodes when inhaled or oral sympathomimetic agents are ineffective in controlling asthmatic symptoms. Epinephrine (1:1000) is very effective in this respect, and the usual dose is 0.3 ml injected subcutaneously; this can be repeated within 30 to 60 minutes.[27] Terbutaline is also available for subcutaneous injection at a recommended dosage of 0.5 mg.[28] If acute bronchoconstriction does not respond to the above adrenergic drugs, aminophylline 4-6 mg/kg iv, injected slowly over a period of 10 to 15 minutes, successfully controls the majority of acute attacks in adults.[29,30] This loading dose should be reduced if the patient has recently received a therapeutic dose of theophylline salts.[29] Parenteral steroids, such as hydrocortisone, may also be required to control acute episodes of refractory asthma.[31]

Pretreatment with the corticosteroid aerosol, beclomethasone diproprionate, has no effect on the immediate response to bronchial challenge, but the late asthmatic response is inhibited.[32] Similarly, systemic steroids block the late asthmatic reaction, but have no effect on the immediate reaction in baker's asthma.[33]

The protective effect of cromolyn sodium on grain-dust-sensitive subjects is well documented, and it is indicated as a prophylactic medication when exposure to grain dust will induce or exacerbate an acute episode of asthma. When used for this purpose, a dose of 20 to 40 mg, given 20 minutes before the anticipated exposure or three to four times daily, will usually prevent the bronchoconstriction response.[33] This treatment has been shown to inhibit both the immediate and the late component of the dual response in baker's asthma, and most of the patients were able to continue with their occupations while on cromolyn therapy.[14,33] However, when asthmatic symptoms can not be controlled successfully with the above drugs, a patient may need to change professions to avoid further contact with the provocative agents.

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KEY WORDS: baker's asthma, grain dust, occupational disease.

ABSTRACT

A 48-year-old black male with no underlying atopy developed asthma after working nine years at a bakery. The attacks of wheezing were preceded by nasal symptoms and usually occurred after several hours of work. Skin testing revealed reactivity to dust, molds, and wheat extracts; serum level of IgE was normal, and a RAST screen to common allergens was negative. A bronchial provocation test using commercial wheat extract was negative, but the same test using the patient's own bakery flour resulted in an immediate positive reaction. The pathogenesis and management of grain-dust-induced asthma are discussed.

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