

Hypersensitivity Lung Disease in the Turkey Raising Industry¹⁻³

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SUMMARY

Two hundred five subjects involved in raising or processing turkeys were surveyed for clinical and laboratory evidence of hypersensitivity lung disease. One hundred forty-two (69 per cent) described respiratory symptoms occurring within 1 hour after working with the birds. Thirteen workers (6 per cent) also reported dyspnea, cough, myalgia, and fever occurring 4 to 8 hours after exposure to turkeys. Sera from 11 per cent of the study population contained precipitating antibodies against turkey serum, whereas 18 per cent of subjects had positive skin tests to turkey antigens. When compared with the group of 63 subjects without complaints, the symptomatic group had a significantly higher prevalence of precipitating antibodies to turkey serum, positive skin tests to both turkey and environmental antigens, elevated IgE levels, and atopic histories. Many of the immediate onset respiratory symptoms were considered to represent type I immunologic reactions, whereas delayed symptoms were thought to represent type III reactions. This study showed that hypersensitivity pulmonary disease may occur in persons working with turkeys and that the delayed reactions closely resembled the same syndrome reported in pigeon and parakeet breeders.

Introduction

The clinical syndrome characterized by cough, chills, fever, and dyspnea developing 4 to 8 hours after inhalation of specific antigens has been termed hypersensitivity pneumonitis, or extrinsic allergic alveolitis (1). Persons with this syndrome frequently demonstrate positive Arthus type skin tests and precipitating antibodies to the offending antigen (1). In recent years, an increasing number of organic materials has been associated with this syndrome (2). Bird antigens were first implicated as a cause of this disease in parakeet fanciers (3, 4) and subsequently, ex-

posure to pigeons (5-8) and chickens (9) was also shown to produce this entity. The disease is thought to be caused by a type III immunologic reaction (10) to antigenic material in bird excreta. Occasionally, the immediate onset of wheezing and dyspnea accompanies the delayed reaction, and these symptoms are caused by a type I immunologic reaction (11).

In 1971, a diagnosis of hypersensitivity pneumonitis was made in a patient exposed to turkeys. Because turkey raising is a large, nationwide industry, we thought it important to in-

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investigate further the occurrence of this syndrome in the turkey industry. This report describes the results of an epidemiologic study of a large group of turkey growers in central Utah.

Case Report

Patient CC, a 36-year-old, white male, was first exposed to turkeys at 16 years of age and has had intermittent exposure to live turkeys and turkey barns since that time. In 1967 he was diagnosed as having pulmonary coccidioidomycosis but recovered uneventfully without therapy. In October 1970, he experienced dyspnea, fever, and myalgia 3 to 4 hours after cleaning a turkey brooder barn. The symptoms resolved within 24 hours, but recurred after his next exposure. In March 1971, he was seen by a physician and had a normal physical examination. The hematocrit, leukocyte count, sedimentation rate, and spirometry were within normal limits. A chest roentgenogram showed bilateral, small, noncalcified nodules, presumably from his previous infection with coccidioidomycosis.

The patient continued to work with turkeys but wore a respirator face mask that prevented these symptoms. In March 1973, he agreed to work in the turkey brooder barn without a protective mask, and he was evaluated 3 hours after stopping work. At that time he complained of dyspnea, dry cough, malaise, and myalgia, none of which had been present before work. Physical examination was within normal limits. Laboratory studies showed a normal blood count, sedimentation rate, spirogram, and carbon monoxide diffusing capacity. A chest roentgenogram was unchanged. A serum specimen was positive for precipitins to turkey droppings and turkey feathers. A skin test using turkey serum (1:100 dilution) showed no reaction at 15 min and at 8 hours.

Materials and Methods

The turkey plant: This study was conducted over a 2-day period at a turkey growers' cooperative in Utah. This organization is composed of approximately 125 members, each of whom raises turkeys independently but has joint ownership of a feed mill, hatchery, and processing plant. Each grower raises between 5,000 and 750,000 turkeys annually. More than 3 million turkeys are processed at the plant each year, and during peak work periods up to 400 persons are employed. All members of the cooperative were notified of the study by mail and by telephone and invited to attend a clinic held at the plant site.

The study population: Two hundred five persons

associated with the turkey industry participated in the study. There were 150 males (12 to 74 years of age; mean age, 41 years) and 55 females (20 to 63 years of age; mean age, 45 years). Of these, 78 were members of the cooperative and 127 were family members of growers or cooperative employees. Twenty-four persons living in the area but not associated with the turkey industry were also studied as a control group.

Questionnaire: A questionnaire was mailed in advance of the clinic date to each member of the cooperative. This questionnaire was designed to evaluate the occurrence, frequency, and characteristics of 15 respiratory and systemic symptoms. Other questions relating to occupation, duration of turkey exposure, smoking, and medical histories were also included. Positive responses were discussed with each subject in a personal interview.

Skin tests: Antigen extracts of various turkey products were prepared by the technique of Sheldon and associates (12). Blood was pooled from 6 adult turkeys, the serum passed through Seitz filters, and sterility assured. Serum was then diluted with 0.9 per cent saline and 0.5 per cent phenol to a 1:100 preparation by volume.

Turkey droppings and turkey bedding (cedar wood shavings) were obtained from a brooder barn and defatted with ether (U. S. P.) for 72 hours before drying. Ten g of each material were then extracted with 100 ml of Coca's Solution, filtered and dialyzed in cellulose casing. Each extract was diluted with Maury's Diluent (Evan's Solution) (Maury Biological Co., Los Angeles, Calif.) to 1:10,000 by volume and tested for sterility.

Eight additional skin testing preparations of common environmental antigens were also used in the following concentrations: (1) major mold mix, 1:10,000; (2) ragweed, 1:10,000; (3) *Candida*, 1:10,000; (4) sage mix, 1:10,000; (5) house dust, 1:1,000; (6) grass mix, 1:10,000; (7) Russian thistle, 1:10,000; (8) pigeon feathers, 1:1,000. Saline, 0.9 per cent, was used as a control skin test.

Each subject was tested for evidence of skin reactivity to the extracts of turkey serum, bedding, and droppings, as well as to the 8 environmental antigens and saline. All tests were performed by a nurse who was experienced in allergy testing. A volume of 0.02 ml of each extract was injected intradermally on the volar surface of 1 forearm of each subject. Tests were interpreted at 15 min by one of us who had no knowledge of the skin distribution of the antigens. Each subject was instructed how to measure and record the tests in 6 hours. Those tests demonstrating a wheal of 8 mm or greater in diameter at 15 min were considered positive immediate reactions and those with induration greater than 10 mm in diameter at 6 hours were considered positive Arthus reactions.

Serologic tests: Serum from each subject was tested for the presence of precipitating antibodies to

turkey serum by the Ouchterlony technique of gel double diffusion (13) and by the method of counter-immunoelectrophoresis (CIEP), as modified by Gocke and Hoe (14). Commercially prepared agar plates and power source (supplied by Hyland Laboratories, Costa Mesa, Calif.) were used. Precipitin reactions with the Ouchterlony technique were measured at 48 hours and scored by intensity and by number of bands (arcs). For the CIEP method, those sera which produced a distinct band were scored as positive. Some sera were also tested by the CIEP technique for antibodies to pigeon serum, parakeet feathers, chicken house dust, *Micropolyspora faeni*, *Aspergillus mix*, *Cryptostroma corticale*, and *Pullularia pullulans* (Hollister-Stier Laboratories).

Determination of IgE immunoglobulin levels was performed on each serum sample by the radial immunodiffusion technique using IgE Immunoplates (Hyland Laboratories) according to the method of Mancini and associates (15). An IgE concentration greater than 800 international units per ml was considered elevated.

Pulmonary function tests: All subjects performed 3 forced expiratory vital capacity (FEVC) maneuvers into a 13.5-liter Collins spirometer. This spirometer was connected to a computer at the Latter-day Saints Hospital in Salt Lake City (120 miles away) for on-line measurements (16), and results were returned to the clinic site on an oscilloscope screen. The measurements included the FEVC, forced expiratory volume in 1 second (FEV₁), and the FEV₁/FEVC percentage. An FEVC of less than 80 per cent of predicted value, and/or an FEV₁/FEVC percentage of less than 75 were considered abnormal.

Chest roentgenograms: A standing 14-by-17-inch posteroanterior chest roentgenogram was taken of each subject in a mobile X-ray unit (Utah State Division of Health). Each roentgenogram was interpreted by a radiologist without knowledge of the clinical history, and all abnormal roentgenograms were reviewed by the authors.

Results

Questionnaire: One hundred forty-two subjects

(69 per cent) described at least 1 respiratory symptom occurring within 1 hour after exposure to turkeys or their habitats. The most common symptoms were nasal congestion (61 per cent), coughing (52 per cent), sneezing (48 per cent), dyspnea (34 per cent), and wheezing (28 per cent). Thirteen of these persons also gave a history of dyspnea, cough, fever, chills, and malaise that occurred 4 to 8 hours after turkey exposure. There was no significant difference in the mean age, sex distribution, years of exposure, smoking history, or allergic background between the groups with immediate and delayed symptoms.

Subjects with and without respiratory symptoms are compared as to 5 variables in table 1. The only real difference between the 2 groups was that the symptomatic group had a significantly higher percentage of persons with a previous allergic history unrelated to turkey exposure.

Skin tests: A significantly higher percentage of subjects with positive immediate and Arthus skin tests to turkey serum were in the symptomatic group as compared to the asymptomatic group (table 2). This group also had a significantly higher percentage of positive reactions to 1 or more of the 8 environmental antigens. Of the 13 subjects with delayed onset symptoms, none had positive Arthus type skin test reactions with turkey serum (1:100 dilution). Skin test results in the control group as compared with the study group are shown in table 3.

Serologic tests: Twenty-three (11 per cent) of the subjects in the study population demonstrated precipitins to turkey serum, whereas none in the control group did. There was also a higher prevalence of precipitins in the symptomatic than in the asymptomatic groups (table 4). None of the sera studied contained precipitins to pigeon serum, parakeet feathers, *Micro-*

TABLE 1
RESULTS OF QUESTIONNAIRE ADMINISTERED TO 205
SUBJECTS EXPOSED TO TURKEYS

Group (No. of Subjects)	Mean Age (years)	Males (%)	Mean Years of Turkey Exposure	Smokers (%)	Allergic History (%)*
Symptomatic (142)	42	65	20	28	40
Asymptomatic (63)	42	69	21	23	11
P value		NS	NS	NS	< 0.001

NS = not significant.

*History of allergic reactions (hayfever, asthma, hives, etc.) not associated with exposure to turkeys.

TABLE 2
SKIN TEST RESULTS IN 205 TURKEY RAISERS

Group (No. of Subjects)	No. Positive to Turkey Antigens* (Serum and/or Droppings) (%)	No. Positive to Turkey Antigens† (Serum and/or Droppings) (%)	No. Positive to Common Environmental Antigens* † (Pollens, Molds, Dusts) (%)
Symptomatic (142)	25 (18)	11 (8)	45 (32)
Asymptomatic (63)	2 (3)	1 (2)	6 (10)
P value	< 0.001	< 0.001	< 0.001

* 15-min reaction (immediate).

† 4- to 8-hour reaction (Arthus).

TABLE 3
SKIN TEST RESULTS IN 205 TURKEY RAISERS
AND 24 CONTROL SUBJECTS

Group No. of Subjects)	No. Positive to Turkey Antigens (Serum and/or Droppings) (%)*	No. Positive to Common Environmental Antigens (Pollens, Molds, Dusts) (%)*
Study group (205)	36 (18)	51 (25)
Control group (24)	1 (4)	7 (29)
P value	< 0.05	NS

NS = not significant.

* 15 min (immediate) and/or 4- to 8-hour (Arthus) reactions.

polyspora faeni, *Aspergillus* mix, *Cryptostroma corticale*, or *Pullularia pullulans*.

Twelve persons (5 per cent) in the study population had elevated IgE levels ranging from 820 to 5,200 international units per ml. Eleven of these were in symptomatic subjects. Elevated IgE levels were not found in those persons with delayed-onset symptoms nor in the control population.

Pulmonary function tests: Twenty-three subjects (11 per cent) had abnormal spirometric measurements, characterized in each case by an obstructive pattern. There were no significant

differences between the symptomatic and asymptomatic groups in the occurrence of abnormal spiograms.

Roentgenograms: Two subjects were identified with abnormalities in the lung fields on chest roentgenograms. They were Patient CC (see case report) and a 59-year-old man with a long history of delayed symptoms after exposure to turkeys. The roentgenogram of his chest revealed bilateral, linear, interstitial infiltrates that were unchanged on a repeat study 9 months later.

Discussion

Hypersensitivity lung disease caused by the inhalation of avian antigens has been reported in persons exposed to parakeets, pigeons, and chickens (4, 5, 9). From our study, it appears that a similar entity also exists with exposure to turkeys. While many of the subjects who reported respiratory symptoms after exposure to turkeys may have experienced nonimmunologic, irritant reactions, our data indicate that both type I and type III immunologic reactions can be implicated in certain persons.

Thirteen subjects (6 per cent) described the delayed appearance of systemic and respiratory

TABLE 4
PRECIPITIN REACTIONS TO TURKEY
SERUM IN 205 TURKEY RAISERS

Group (No. of Subjects)	No. Positive to Turkey Serum (%)	P Value
Asymptomatic (63)	3 (5)	< 0.01
Symptomatic (142)	20 (14)	
Delayed-onset symptoms (13)	3 (23)	NS
Immediate-onset symptoms (129)	17 (13)	

NS = not significant.

symptoms after exposure to turkeys or related products. These symptoms were similar to those reported in pigeon breeder's disease. When Patient CC was challenged by working in his turkey barn without a face mask, he developed dyspnea, cough, and myalgia several hours later. His sera also contained precipitins to turkey antigens. A second subject had a long history of delayed-onset symptoms after working in turkey fields or barns and a chest roentgenogram revealing a chronic, interstitial infiltrate. This case may represent the more insidious and chronic form of pulmonary hypersensitivity reaction (17, 18).

Previous studies in persons who raise pigeons have shown that between 14 per cent and 40 per cent of those engaged in this hobby will have precipitating antibodies against pigeon serum (8, 19). In this study, 11 per cent of subjects had precipitins to turkey serum and there was a significantly higher percentage of precipitins in those with symptoms (14 per cent) than in those without symptoms (5 per cent). The occurrence of precipitins in asymptomatic persons is in accordance with previous studies in pigeon breeders (19) and indicates that a positive precipitin test alone does not establish the diagnosis of hypersensitivity lung disease (20, 21). Only 3 of the 13 subjects with delayed-onset symptoms had serum precipitins, a lower prevalence than described in persons with pigeon breeder's disease. This may be explained by the fact that in many cases the symptoms were relatively mild, in contrast to reports of other bird raisers with this syndrome when only acutely ill persons who had sought medical care were evaluated. In addition, many of our subjects with delayed-onset symptoms had experienced these for several years. It has been shown in other hypersensitivity diseases, such as farmer's lung, that only 53 per cent of those affected retain precipitins to the offending antigen in the chronic stages of the disease (18). It is also possible that a different antigen was responsible for these symptoms that was not identified by our serologic techniques.

Although a significantly higher percentage of symptomatic persons had positive immediate skin tests to turkey antigens, none of the 13 subjects with delayed-onset symptoms demonstrated positive Arthus skin tests. However, for this study we used diluted turkey serum (1:100) as the skin test antigen as a precaution against serious allergic reactions occurring at the clinic site. Hargreave pointed out previously that serum di-

lutions of 1:10 and 1:100 may be too weak to elicit an Arthus reaction and that only undiluted sera would consistently give positive responses in symptomatic bird breeders (4). This may account for our low prevalence of positive Arthus skin reactions.

It has been shown previously that the immediate occurrence of respiratory symptoms after avian exposure might be caused by an IgE mediated (type I) reaction (11). There is evidence from this study to suggest that a number of persons had experienced type I allergic responses after exposure to turkeys. For example, 116 subjects reported symptoms of sneezing, nasal congestion, or wheezing after turkey exposure. Of the 142 symptomatic subjects, there was a significantly higher percentage of persons with histories of non-turkey allergies and with all types of positive skin tests, when compared to the asymptomatic group. In addition, 11 of the 12 persons with elevations of IgE antibody were from the symptomatic group. These findings suggest that type I hypersensitivity reactions had occurred in many of the subjects exposed to turkeys.

Clinical surveys have been done in other groups of bird raisers. Fink (19) found that 15 per cent of 200 pigeon breeders experienced respiratory symptoms occurring after exposure to pigeons, and Elman (22) found that 20 per cent of 58 chicken farmers described chest tightness and cough after prolonged exposure to chickens. The higher incidence of pulmonary symptoms in the turkey growers may, in part, be explained by the greater concentration of airborne irritants and by the more frequent and prolonged exposure to which the workers may be subjected.

Twenty-three (11 per cent) of our subjects had abnormal spirometry of the obstructive type, and 2 of the 13 subjects with delayed symptoms had mild obstructive disease. No turkey workers had restrictive lung disease. Fink (19) reported a similar percentage of abnormal spirometry in 200 pigeon growers. However, this prevalence of obstructive airway disease is no different from that observed in general population surveys (23, 24), and no association can be made between turkey exposure and abnormal spirometry.

The findings of this study suggested that the inhalation of dust containing turkey feathers, bedding, or droppings can produce immunologic reactions in the lung similar to those seen in pigeon and parakeet raisers with hypersensitivity pneumonitis. The prevalence of this syndrome and of other respiratory symptoms asso-

ciated with bird exposure in turkey raisers appears to be slightly higher than that observed in persons exposed to chickens or pigeons. The possible progression of this disease to pulmonary fibrosis is suggested by one case. In affected subjects, avoidance of the offending dust or the use of mask respirators is suggested.

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