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MID-AMERICA DAIRYMEN, INC.
MONETT, MISSOURI

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I. SUMMARY

On March 27, 1986, the National Institute for Occupational Safety and Health (NIOSH) received a request from Mid-America Dairymen, Inc. to evaluate respiratory illness that occurred in five workers between August 1985 and March 1986 at their whey processing plant in Monett, Missouri. Between August and November 1985, four of the five employees developed an illness characterized by dry cough, chest tightness, fatigue, shortness of breath, and weight loss. Of these five workers, four were diagnosed with hypersensitivity pneumonitis (HP) and one was diagnosed with asthma.

On May 28 to 29, 1986, NIOSH investigators conducted an initial walk-through survey at the Monett plant. Personal (breathing zone) and area air samples were collected for hydrochloric acid (HCl) released during bulk acid unloading at the plant. The one personal air sample had a time weighted average (TWA) concentration of 0.44 milligrams per cubic meter (mg/m^3). Concentrations of HCl from five area air samples ranged from not detectable (ND) to 0.21 mg/m^3. The Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) and the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV*) for HCl is 7 mg/m^3 for a 15-minute exposure based on the substance's irritant properties. There is no NIOSH Recommended Exposure Limit (REL) for HCl.

To identify aerosolized microbiological species which may have led to the development of respiratory illness, air samples were collected from different areas of the plant during follow-up visits and tested for growth of fungi, thermophilic actinomycetes, and mesophilic bacteria. Area samples were collected at a location formally used for electrodialysis (ED) stack maintenance, a job performed by the four employees diagnosed with HP. Samples were also collected in the pasteurization and whey separation rooms, and at locations outside the plant.

Air sample analysis for viable organisms showed that the fungal bioburden at the Monett plant, in the areas where samples were collected, fell in the following five common environmental mold genera: Cladosporium, Penicillium, Fusarium, Alternaria, and Aspergillus. The lowest total fungal count (169 colony forming units (CFU)/m^3) was obtained in the former stack maintenance room, reflecting the low activity level in this area. The pasteurization room, where stack maintenance is currently performed, registered the highest fungal count (1,746 CFU/m^3). Bacteria and thermophilic actinomycetes identified in the air samples included Micrococcus, Streptomyces, and Bacillus. Although no authoratative evaluation criteria for acceptable exposure to microbiological aerosols currently exist, the ACGIH Committee on Bioaerosols has proposed a total viable microorganism count of 10,000 CFU/m^3 or more, or colony counts of any one species of fungus, actinomycetes, or bacteria in excess of 500 CFU/m^3, as requiring remedial action.

Cultures were obtained from bulk samples of cheese curd, whey, and membrane stack deposits. A heavy growth of Geotrichium sp. and Candida sp. were identified from the stack deposit cultures. Penicillium roqueforti quickly overgrew cheese curd samples collected at the plant and allowed to spoil in a sterile container at room temperature.

The workers who became ill during the fall and winter of 1986 were interviewed, as were their physicians. A complete diagnostic profile was not available on all workers; however, abnormal blood gas, X-ray, and pulmonary function tests supported the diagnosis of HP. The occurrence of Immunoglobin G (IgG) antibodies (precipitins) to Penicillium camemberti in blood samples of three of the four workers suggested exposure to aerosolized mold spores which may be responsible for the illnesses.

A questionnaire, completed by 74 of 75 employees at the plant in August 1986, identified seven (9%) of the participants as cases, defined as four or more symptoms compatible with HP, and 61 (82%) as non-cases, defined as the presence of no more than one symptom. Six workers (8%) reported two to three symptoms.

The sera from 75 workers were tested for precipitins to 22 antigens, including samples of stack deposits, dust, milk and whey protein, Thermophile and Penicillium sp. The prevalence of IgG precipitins to individual antigen samples varied from 100% to zero. The prevalence of precipitins to Aspergillus fumigatus (100%) and Bacillus sp. (80%) was unusually high. Control serum from one of the NIOSH investigators was also positive for Aspergillus fumigatus and Bacillus sp., suggesting that nonspecific binding was responsible for the presence of precipitins in these two antigen extracts. All seven cases had precipitins to at least one antigen, compared with 15 of 61 non-cases (odds ratio undefined, p=0.0002, Fisher's exact test). Two cases with multiple precipitins were among the first three stack maintenance workers to be diagnosed with HP.

NIOSH investigators determined that illness among stack maintenance workers was most likely related to aerosolization of organic deposits on the electrodialysis membranes during cleaning. Membrane stacks waiting to be cleaned can provide an ideal growth medium for many microbiological species. Air samples collected during electrodialysis stack maintenance showed a marked increase in viable airborne microorganisms; non-viable proteins were likely to have been increased as well. Biological and environmental studies were not able to identify a specific agent or antigen responsible for illness in these workers. However, air samples collected in August 1986 may not have adequately represented exposure conditions during the previous fall and winter, and antibody levels in workers may have decreased during this time. Ventilation for the electrodialysis stack maintenance operation is discussed in detail in Section VII. Recommendations for other engineering and work practice changes, and for periodic medical monitoring for stack maintenance workers, are included in Section IX.

KEYWORDS: SIC 2026 (Fluid Milk), hydrochloric acid, mold, electrodialysis, viable air sampling, bioaerosols, fungi, bacteria, thermophilic actinomycetes, ventilation, hypersensitivity pneumonitis.

II. INTRODUCTION

On April 2, 1986, NIOSH received a request from management at Mid-America Dairymen, Inc., a company headquartered in Springfield, Missouri, concerning respiratory illness in five workers between August 1985 and March 1986 at their whey processing plant in Monett, Missouri. Four of these five employees became ill between August and November 1985 (two reported symptoms in August, one in October and one in November 1985). Illness in these four workers was characterized by dry cough, chest tightness, fatigue, shortness of breath, and weight loss. The fifth worker, who first became ill in February 1986, reported similar symptoms, but also experienced nocturnal chills and fevers. Four of six full-time employees in the electrodialysis (ED) stack maintenance department were diagnosed with hypersensitivity pneumonitis (HP). One worker, from among 12 in the cheese finishing department, was diagnosed with asthma. All five of the above employees went on extended medical leave following their illnesses.

On May 28-29, 1986, NIOSH investigators conducted an initial walk-through survey at the Monett plant. Production records were reviewed, a questionnaire was administered to identify other workers who experienced symptoms, environmental air sampling for hydrochloric acid (HCl) mist was performed, and a sero-prevalence survey for immunoglobin G (IgG) precipitins was conducted to identify exposure to antigens isolated at the plant. A follow-up visit was performed on August 6-8, 1986 to conduct air sampling for viable organisms, administer a medical questionnaire, and collect blood samples to test the seroprevalence of antibodies to organic antigens isolated at the plant. A second follow-up visit was conducted on December 2-4, 1986 for additional medical and environmental sampling.

Mid-America Dairymen operates a smaller whey processing plant in Fergus Falls, Wisconsin. However, employees at this Wisconsin facility have not reported similar health effects. The Fergus Falls plant utilizes a slightly different stack membrane cleaning technique which involves a large water vat in which the ED membranes are completely submerged prior to manual rinsing with a water spray to remove membrane deposits. In contrast, employees at the Monett plant clean the ED membranes on a work table, followed by a high powered water spray to dislodge and remove membrane deposits. Electrodialysis stack maintenance is described in more detail in Section III.

III. BACKGROUND

A. History of Problem

From August 1985 to March 1986, four employees involved in cleaning and maintenance of equipment used in whey demineralization at the Mid-America Dairymen plant in Monett, Missouri, developed a dry, non-productive cough, exertional dyspnea, anorexia, and weight loss ranging from 10 to 25 pounds. Affected workers were male, between 23-35 years old and previously reported to be in excellent health. A complete diagnostic profile was not available on all workers; however, abnormal blood gas, X-ray, and pulmonary function tests supported the diagnosis of allergic alveolitis, or HP. A lung biopsy from one of the workers revealed multiple granulomas with lymphocytic, plasmocytic infiltrates, characteristic of interstitial lung disease. Immunological studies identified IgG antibodies (precipitins) to Penicillium camemberti in three of the four workers, suggesting that exposure to aerosolized mold spores may have been responsible for illness. All four workers were involved in "stack maintenance", the manual disassembly and cleaning of ED membranes used in the demineralization (purification) of raw whey. The fifth worker, who reported symptoms and was diagnosed with asthma, worked in the cheese processing area of the plant.

The three stack maintenance workers experiencing symptoms between August and November 1985 went on medical leave in November of that year. One of the replacement workers, who started in November 1985, began reporting respiratory symptoms the following February. In all, from August 1985 to February

1986, four of six full-time stack maintenance workers developed respiratory illness. Although complete diagnostic profiles are not available, radiographic evidence of interstitial lung infiltrates in three of the workers, decreased pulmonary diffusion capacity tests in two, and trans-bronchial biopsy results in one worker, support the diagnosis of HP.

Initially, employees were concerned that workplace exposure to hydrochloric acid (HCl) was responsible for their illnesses. Approximately 750 to 900 gallons of concentrated HCl (38% acid) is used per 24 hour period to demineralize the whey. The Occupational Safety and Health Administration (OSHA) investigated employee exposures to HCl during a plant inspection in January, 1986. Although no workers were exposed to excessive HCl concentrations, high HCl levels (550 ppm), indicative of a potential overexposure situation, were measured in an area air sample collected from an unoccupied acid tank storage room. The absence of a wet scrubber control system on the acid tank vents at the time of the OSHA survey (since installed by Mid-America) accounted for the extremely high acid concentrations.

Stack maintenance had been performed in a small (10 x 20 x 10 feet) room equipped with a ceiling mounted fan coil unit which recirculated 100% of the room air. In retrospect, NIOSH investigators believe this area lacked an adequate supply of fresh make-up air. Management responded to the illnesses in November 1985 by dismantling, steam cleaning, and then replacing the recirculating fan coil unit. At the time of its removal, the filter on the fan coil unit was reported by both management and employees to be heavily coated with slime. Unfortunately, no samples were collected from the fan coil unit during its removal to characterize the microbiological contamination. While the ventilation unit was being replaced, the stack maintenance process was moved to the adjacent pasteurization room (approximately 40 x 60 x 10 feet high) at the end of November 1985. A plant schematic is shown in Figure 1.

Despite these changes, in February 1986 a stack maintenance worker, a replacement for one of the three stack workers who had become ill in November 1985, also developed symptoms. This worker reported nocturnal episodes of chills and fevers (which correlated with ED membrane cleaning activities during the daytime) as well as dry cough, shortness of breath, chest tightness and weight loss.

B. Process Description

The two-story facility employs approximately 75 workers in the production of cheese curd, whey protein, and powdered milk. Over one million pounds of milk are processed daily, of which 10% becomes cheese curd and 25% becomes purified (demineralized) whey. Raw milk is pasteurized, inoculated with rennet and a cheese starter mix, and allowed to curdle. The sweet curd is transported, via pipe, to an adjacent plant (not owned by Mid-America Dairymen) for processing into cheese. Whey, the liquid by-product of cheese production, contains approximately 6% solids. To recover the whey solids, which are used as a protein supplement in baby food, the whey is concentrated, repasteurized, and then demineralized using tortuous-path ED membranes.

Unlike some methods of cheese production (for example, bleu and roquefort cheeses), no fungal cultures are used or needed in the production of cheese curd. Potential sources of fungal growth identified at the plant are whey deposits on the ED membrane stacks waiting to be cleaned. The membranes require constant exposure to water when not in use, and although they may provide a suitable environment for fungal growth, the fungi would not be expected to have the opportunity to dry out and aerosolize.

There are 16 plants world-wide which use ED to purify whey; four are located in United States. At this plant the ED process has run unchanged since approximately 1983 without instances of the illnesses described in this investigation. Cheese washers lung, or

cheese workers disease, has previously been reported due to Penicillium sp. used in or contaminating cheese production.[1,2] It has seldom been reported in the United States because of differences in the cheese aging process, and it has not been reported in workers involved in whey purification.

Demineralization of the whey is accomplished by tortuous-path ED membranes. A typical ED membrane, shown in Figure 2, is assembled into "stacks" composed of two hundred alternating cation and anion exchange membranes, separated by spacer gaskets. The 18- by 40-inch membranes are manufactured by Ionics Inc., Watertown, MA. The whey is pumped from a holding tank to the stacks via pipes located at the top of the stack assembly. A direct current of 440 volts is applied across the stack as the liquid whey flows through thin (40/1000 inch) channels formed when the membranes are placed ("stacked") on top of each other. Excess calcium and magnesium ions selectively move through the membranes into the brine waste stream. Whey solids, which do not pass through the membranes, are collected in the demineralized product stream.

Three ED stacks comprise a production line (referred to as a "skid"). At the Monett plant there were four skids, of which three were used in regular production runs and one used for prototype set-ups. The ED process operates continuously, and approximately 250,000 pounds of whey are demineralized daily.

The raw whey, brine waste, and demineralized product streams enter or exit the stack through pipes, permitting the entire assembly to be cleaned in place. Periodically, the thin membrane channels become clogged with proteinaceous materials and calcium carbonate deposits, requiring "stack maintenance" to remove this material.

After a membrane stack has been on line for approximately 10 days, it is replaced with a new "clean" stack. The used ("dirty") stack is moved to an adjacent maintenance room for manual disassembly and cleaning, which is performed in two stages. In the first stage, membranes are cleaned in place with sequential flushing of water, 5% sodium hydroxide solution, water, hydrochloric acid, and water. In the second stage, stack maintenance involves manual removal of the remaining deposits and inspection of the individual membranes by up to three workers. A utility knife is used to scrape deposits at the edges and a fibrous pad is used to clean the delicate surfaces of the membranes. A high-pressure water jet is used to further loosen and remove the scraped material from the surface. Individual membranes are inspected for wear, and damaged and defective ones are replaced. The ED membranes, to avoid damage, are not permitted to dry out (new membranes are stored in propylene glycol until used). Disassembly, cleaning, and reassembly of a stack can take three to four workers two days to complete. In addition, dirty stacks may wait two to four days (or longer) before being disassembled and cleaned.

C. Building Ventilation

There are no local exhaust ventilation systems used by the Monett plant. Instead, general ventilation is provided by intake and exhaust fans situated in the large processing rooms located on the perimeter of the building (pasteurization, electrodialysis, evaporation, and whey separation rooms). These large propeller fans, located in both the walls and ceilings, are manually controlled. During colder months the fans would generally not be operated in order to reduce heating costs by taking advantage of the heat generated by the processing equipment. Ceiling-mounted steam space heaters, located in several of the processing areas, are seldom used.

Ventilation for the former location of the stack maintenance operation (until November 1985) consisted of a fan-coil unit, installed in a suspended ceiling, which essentially recirculated the room air without bringing in fresh, outside air. A diagram of a typical fan coil system is shown in Figure 3. This unit was replaced in November 1985 following the first reports of health effects in the stack maintenance workers. The new air-conditioning system for this area, installed in December 1985, draws air from a hallway adjacent to the room.

IV. EVALUATION DESIGN

A. Environmental

1. Initial Site Visit

Air samples (5 area, 1 personal) were collected for hydrochloric acid (HCl) mist on May 28, l986, during the unloading of approximately 2,600 gallons of concentrated HCl (38% HCl) from a tanker truck to acid storage tanks located on the roof of this three-story plant. This unloading process, requiring 1.5 hours to complete, was performed after several modifications, designed to minimize HCl exposure to the surrounding plant areas, had been installed by the company. These changes included the use of a dual diaphram pump (instead of compressed air) to transfer acid to the roof storage tanks and the routing of all acid tank vents through a wet scrubber (instead of direct venting to the atmosphere). Only one worker was potentially exposed to acid mist during the bulk unloading process.

Air sampling was conducted during the bulk unloading of acid (approximately 90 minutes) using activated silica gel sorbent tubes (ORBO 53) and a sampling flowrate of 200 cubic centimeters of air per minute. The sampling and analytical method used was NIOSH Method No. 7903 for inorganic acids. Analysis for the chloride ion was by ion chromatography, and the limits of detection and quantitation for this sample set were 1 and 3 micrograms of chloride per sample, respectively.

2. Follow-up Survey, August 6-7, 1986

During the first follow-up evaluation area air samples were collected for fungi, thermophilic actinomycetes, and bacteria using both Anderson two-stage and N-6 (modified single-stage) viable samplers following the protocol outlined in this section. Sampling times of 5 and 15 minutes for the two-stage samplers, and 5 minutes for the N-6 sampler, were selected. The 5-minute sampling period for the N-6 sampler was chosen since overloading this sample was more likely with only one media collection plate. Four different areas (three inside, one outside the plant) were monitored--whey separation, stack maintenance (former location), pasteurization (new location of stack maintenance), and outside the plant--using both two-stage and NIOSH-6 (N-6) viable air samplers. The samples were subsequently cultured and identified at a contract microbiology laboratory in Columbia, Missouri.

A NIOSH research chemical engineer participated in the follow-up survey to review the ED membrane cleaning techniques and the ventilation systems at the Monett plant. A number of ventilation control alternatives were considered by NIOSH for controlling aerosols potentially generated in the stack maintenance procedure. These control alternatives, discussed in Section VII, included: (1) a backdraft, multiple slot hood similar to a welding bench; (2) a push-pull design consisting of a downdraft hood located below the working surface; and (3) a booth in which air is uniformly supplied at the top and exhausted at floor level. The object was to select an appropriate engineering control to decrease the inhalation hazard to employees by removing proteinaceous materials generated during membrane cleaning.

3. Second Follow-up Survey, December 3, 1986

On December 3, 1986 air samples were again collected for three classes of microorganisms, including fungi, thermophilic actinomycetes, and bacteria, both before, during, and after the ED stack cleaning process was performed. Samples were collected, using two-stage viable samplers and a sample time of 5 minutes, from the pasteurization room and outside the plant.

4. Viable Air Sampling Methodology

The sampling protocol and analytical procedures used in this evaluation were basically consistent with those outlined by the ACGIH Committee on Bioaerosols.[3] Air sampling for viable microorganisms was conducted using two methods. The first, using the two-stage Anderson Viable Particle Sizing Sampler, is designed to separate airborne microbial contaminants into two fractions, respirable and nonrespirable, as well as obtaining a total count of airborne microorganisms. The two-stage sampler separates particles into two size ranges, with the 50% cut-off diameter of the first stage set at 8 microns (u) for spherical particles of unit density. The second method, referred to as NIOSH-6 (N-6) sampler, is a modified single-stage version of the standard 6-stage Anderson Viable Particle Sizing Sampler.[4] Examples of the complete 6-stage Anderson Sampler, and the modified N-6 sampler, are shown in Figure 4.

All air samples were collected on 100 millimeter (mm) x 15 mm disposable plastic Petri dishes (plates) containing either 20 milliliter (ml) of culture media (for two-stage samplers) or 45 ml of culture media (for the N-6 samplers).[3,4] Air samples were collected by placing media plates into the viable air samplers, the agar surface being situated at a fixed distance from orifices through which ambient air is introduced.

In the N-6 sampler, one culture plate was placed on top of the instrument base plate (spring clamp removed) and the sixth stage was then sealed to the base plate using electrical tape. For the two-stage samplers, two culture plates were used. The standard Anderson inlet was not used with either sampler. Both the two-stage and N-6 samplers were connected to vacuum pumps calibrated to provide an air flow of 28.3 liters per minute (lpm) through the samplers.

The media used for the detection of fungi consisted of V-9 agar, a mixture of potato dextrose agar and V-8 juice.[5] Trypticase soy agar was the media used to detect both thermophilic actinomycetes and bacteria.[3] Fungi and bacteria/thermophilic actinomycetes air samples were collected for 5 and 15 minutes at each location during sampling performed on August 6-7, 1986. "Bracketing" of sampling periods was done for this first follow-up survey to ensure that at least one of the culture plates would contain colonies within a range suitable for accurate counting. On the second follow-up survey (using only two-stage samplers) air samples were collected for 5 minutes. To avoid potential cross-contamination of samples, the samplers were sterilized after each use by immersing them in 70% isopropanol for at least one minute, then allowing them to air dry.

All culture plates were kept refrigerated before and after use. At the completion of each site visit, the samples were placed in insulated shipping containers and sent, via overnight express service, to a microbiology laboratory to incubate and speciate the samples.

Upon receipt at the lab, the samples were incubated, with temperature and duration of incubation differing for each of the three classes of microorganisms. Fungal samples were incubated at 25°C for nine days; thermophilic actinomycetes samples at 50°C for five days; and those for bacteria at 35°C for two days. Enumeration and speciation was performed at the end of the incubation period.

B. Medical

1. Medical Questionnaire Survey

To determine if other production workers had recently experienced allergic respiratory symptoms, workers completed a medical questionnaire on August 3-4, 1986. Information was requested on work history, medical history, hobbies, and medical symptoms experienced within

the preceding two years. If symptoms were reported, further information was requested on the date of onset, the number of episodes, and the time of the day and week when symptoms occurred. For the purpose of this investigation, illness was defined as a history of at least four of six symptoms compatible with allergic lung disease, between January 1984 and August 1987.

Because many employees worked in the stack maintenance department part-time after the first three stack maintenance workers went on medical leave, job title was not an accurate indicator of employees who had cleaned membranes. Therefore, a second questionnaire was administered on December 3-4, 1986, to obtain detailed information on exposure to ED membranes. Information was requested on the year and length of time the participant worked cleaning the electrodialysis membranes. Self-reported exposure to the stack membranes were used to identify workers with potential exposure to aerosolized particles generated during the stack membrane cleaning process.

2. Precipitin Sero-prevalence Survey

To investigate differences in exposure to aerosolized organic proteins found at the plant, and to commercial isolates of organic proteins previously identified as capable of causing HP in cheese workers, a seroprevalence survey was conducted. Comparison of seroprevalence of precipitins to a particular antigen, or antigen mixtures by exposure (cleaning the stack membranes), was used to identify potential agents responsible for illness. Blood samples were drawn from workers after they completed the questionnaire. The blood samples were allowed to clot, then centrifuged. The serum supernate was decanted into plastic vials, which were then sealed and frozen.

Sera from 74 workers were tested for precipitins to 24 antigens by a contract mycology laboratory blinded to the exposure status of the samples. Sera was tested for IgG antibodies to extracts of 18 antigens isolated at the plant and to four commercial antigen extracts previously reported to be capable of causing HP in cheese workers. Two negative control extracts were included in the antigen panel to test for cross-reactivity to the fungal growth media (V-9) and the thermophilic and mesophilic bacterial growth media (trypticase-soy agar). The antigens are listed in Table 1.

The same mycology reference laboratory used for culturing the air samples isolated and identified microbiological species, and then created antigen extracts from these isolates. The presence of serum antibodies specific for the antigen extracts was tested using a variation of the exoantigen test.[6,7] Immunodiffusion plates consisted of six equidistant 3-mm wells surrounding a central 3-mm well. Serum samples were placed in the central well, while antigen extracts were placed in the surrounding wells. Four similarly designed plates were used for each study participant to allow sampling of 24 antigens. A 10-fold concentration of antigen was achieved by using a Minicon B-15 macrosolute concentrator manufactured by Amicon*.

After inoculation, plates were incubated at 25ºC for 24 hours, refrigerated, then allowed to incubate another 24 hours at 4ºC before precipitin lines were read.

3. Other Studies

In August and December 1986, maintenance and production records were reviewed, and workers were interviewed to identify changes in production that may have precipitated illness in the fall of 1985 and to validate anecdotal reports of increases in the quantity of stack deposits both

preceeding and during the episodes of illness. Stack maintenance log sheets for January 1985 to November 1986 were reviewed. These sheets were used by employees to record the number and type of damaged or worn-out ionic membranes replaced during stack cleaning. Comments about the condition of the stacks, such as "dirty" or "slimy", were also recorded. The percent of membrane stacks reported to be "dirty" by stack cleaners in 1985 is shown in Figure 5.

Records of cheese yield by month, from May 1983 to June 1986, were also reviewed, as were records on the percent of ED solids removed during the period beginning before illnesses were reported. Since workers reported unusual weather conditions during the fall of 1985, local climatological data for Springfield, Missouri in 1985 and 1986 was abstracted from the National Oceanic and Atmospheric Administration's National Climatic Data Center. This climatological data is presented in Figure 6.

Bulk samples of cheese curd, whey, and ED stack deposits (previously collected and refrigerated by workers) were sent to the previously mentioned mycology reference laboratory for culturing.

Medical evaluations were conducted in December 1986 on the three full-time stack maintenance workers to catalog their current health status and to obtain baseline medical data. Because these workers were at an unknown risk of illness, pulmonary function tests, X-rays, blood tests, and carbon monoxide diffusing capacity tests were performed at a local medical clinic.

V. EVALUATION CRITERIA

A. Environmental

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Criteria Documents and recommended exposure limits (RELs), 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLV*s), and 3) the U.S. Department of Labor (OSHA) permissible exposure limits (PELs). Often, the NIOSH recommendations and ACGIH TLV*s are lower than the corresponding OSHA PELs. Both NIOSH RELs and ACGIH TLV*s usually are based on more recent information than are the OSHA standards. The OSHA PELs also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH RELs, by contrast, are based primarily on concerns relating to the prevention of occupational

disease. In evaluating the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet those levels specified by an OSHA standard.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8- to 10-hour workday. Some substances have recommended short-term exposure limits or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high short-term exposures.

1. Viable Organisms and Air Monitoring

Although no evaluation criteria exist for airborne microorganisms, guidelines concerning the significance of different airborne concentrations are beginning to be developed. NIOSH investigators have, through work addressing airborne microbial contamination in office buildings, suggested that a level of viable microorganisms in excess of about 1000 colony forming units per cubic meter of air (CFU/m^3) indicates that the indoor environment may be in need of investigation and improvement.[8] It should be noted that this "action" level does not discriminate between the different classes of microorganisms (bacteria, fungi, actinomycetes), nor does it represent a fine line between safe and hazardous air concentrations. Essentially this level represents a threshold at which further evaluation is recommended. This guideline has limited applicability in industrial settings.

The ACGIH Committee on Bioaerosols, in their draft protocol for monitoring airborne viable microorganisms in office environments, has proposed a total count of 10,000 CFU/m^3 or more as necessitating remedial action.[3] They indicate that remedial action would be necessary if the colony counts of any one specie of fungus, bacteria, or thermophilic actinomycetes were in excess of 500 CFU/m^3. Although this level is applied to all three classes of microbes, it was primarily based on research showing that airborne levels of thermophilic actinomycetes in excess of 500 CFU/m^3 were associated with outbreaks of hypersensitivity lung illness.[3]

2. Hydrochloric Acid

Hydrogen chloride (HCl) gas is a strong irritant of the eyes, mucous membranes, and skin. On release to the atmosphere it readily combines with water vapor to form an irritating acid mist. The major effects of acute exposure are usually limited to the upper respiratory tract and are sufficiently severe to encourage prompt withdrawal from a contaminated atmosphere.[9] Exposure to HCl gas immediately causes cough, burning of the throat, and a choking sensation. Effects are usually limited to inflammation and, occasionally, ulceration of the nose, throat, and larynx.[9] Acute exposures causing significant trauma are usually limited to people who are prevented from escaping. In such cases, laryngeal spasm or pulmonary edema may occur.[10] High concentrations of the gas may cause eye irritation and prolonged or permanent visual impairment, including total loss of vision.[10] Exposure of the skin to a high concentration of HCl will cause burns; repeated or prolonged exposure to dilute solutions may cause dermatitis. Erosion of the exposed teeth may occur from repeated or prolonged exposure.[10]

The current ACGIH TLV and OSHA PEL for HCl is 7 milligrams per cubic meter (mg/m^3) as 15 minute ceiling value.[11,12] There is no NIOSH REL for this substance.

B. Medical

1. Hypersensitivity Pneumonitis

HP, or allergic alveolitis, is a lung disease resulting from sensitization and recurrent exposure to a variety of inhaled particles, most commonly organic proteins. Examples of particles capable of causing HP include mold spores, thermophilic actinomycetes, animal proteins such as avian droppings, and even certain chemicals such as toluene diisocyanate and phthalic anhydride. The characteristic common to all these agents is their immunogenicity (allergenicity), or capability of evoking an immune response in the host.[13,14,15].

Larger particles, such as ragweed or pollen, can also act as allergens and often result in episodes of asthma or hay fever. Asthma and hay fever are often characterized by the presence of high levels of circulating immunoglobin E (IgE) antibodies produced in response to antigen exposure. Symptoms associated with asthma are caused by the stimulation of IgE antibodies which attach to cells (mast cells) in the respiratory system.

HP is also an allergic illness; however, symptoms in HP are not caused by stimulated IgE antibodes. The mechanism of disease and the response by the immune system in HP is more complex than for asthma. IgG antibodes play a role in the development of HP but increased levels of IgG antibodies are not always found in symptomatic individuals. Illness is dependent on other immunologic mechanisms beyond IgG antibody production.[13,16] Many farmers, for example, develop IgG antibodies specific for mold, yet never develop mold spore-mediated HP, often referred to as "farmer's lung".[17,18,19] Furthermore, not all farmers who develop farmer's lung have circulating IgG antibodies. Review of the role of IgG precipitins in HP suggests that while IgG antibodies correlate with antigen exposure, they are not a mediator, indicator, or predictor of disease.[20,21] Much is still unknown about the risk factors which determine why only some individuals develop antibodies or illness after exposure to an antigen.

HP in cheese workers most commonly results from exposure to aerosolized penicillium spores, select species of which may be used to impart characteristic flavor and texture (ripening) of roquefort, camembert, bleu, and other cheeses. Cheese washer's disease (cheese washer's lung) has been reported after exposure to Penicillium roqueforti and Penicillium casei.[22,23] Penicillium species are well adapted for growth on cheese products and will quickly dominate, suppress, and overgrow competing organisms.

Two general forms of HP are recognized. The acute form generally occurs in individuals intermittently exposed to a high dose of antigen or organic protein. Symptoms begin from 4 to 8 hours after inhalation of the antigen. Fever, chills, malaise, dry cough, and dyspnea (labored breathing) occur, gradually subsiding over the next 18 hours. Fatigue may persist for several weeks, and with repeated exposure, anorexia (loss of appetite) and weight loss is common.[22] The chronic form of the disease can occur with continuous exposure to low levels of the antigen. The onset of symptoms is more insidious, and chills and fever occur less commonly. Therefore, intensity and duration of antigen exposure determine the form of illness which develops. Individual host factors are also important.

With continued antigen exposure, symptoms can progressively worsen, leading to pulmonary disability and, in some cases, death.[22] In some patients the disease may progress even after exposure to the offending antigen has stopped. For this reason, once HP has been diagnosed the following medical management is recommended: 1) identification of probable antigen, 2) avoidance of antigen exposure, and 3) medical follow-up, using pulmonary function tests, oximetry studies, and carbon monoxide diffusing capacity (transfer factor) tests to chart the patient's recovery.

Development of HP, like all allergic diseases, depends on individual genetic factors, history of prior exposure to the antigen, and duration and dose of antigen exposure. In some presentations, the disease is easily confused with certain types of pneumonia. Diagnosis is dependent on the history of exposure to potential antigens and the temporal pattern of the disease. The diagnosis is often made after excluding other illnesses and by accumulating findings from physical exams, lung function studies (PFT's and diffusing capacity tests), chest X-rays, and bronchoalveolar washings. Lung biopsies are not justifiable in most cases, but can provide important diagnostic information.[22] The presence of precipitating antibodies against environmental organic antigens can be used to support, but not confirm, the diagnosis of HP.[20]

VI. RESULTS

A. Environmental

1. Initial Site Visit

Concentrations of HCl for the five area air samples ranged from nondetectable (ND) to 0.21 mg/m^3, while the concentration of HCl from the personal air sample was 0.44 mg/m^3. The limit of detection (LOD) for this sample set was 1.0 microgram per sample.

Air sampling for HCl had been conducted by OSHA prior to modifications to the acid transfer system and acid tank vents. Concentrations of HCl measured by OSHA ranged from 0.4 ppm (personal sample) to 550 ppm (area sample in an unoccupied, restricted access, acid tank room). The unusually high area air concentration of HCl (550 ppm) probably reflects the absence of the wet scrubber system on the acid tank vents at the time of the OSHA investigation. The current OSHA and ACGIH evaluation criteria for HCl are 7.0 mg/m^3 (equivalent to 5 ppm) for a 15-minute exposure. There is no NIOSH REL for this substance.

Although the air samples collected on May 28 were not 15-minute ceiling samples, it is unlikely, for at least two reasons, that workers are exposed to concentrations in excess of the OSHA PEL of 5 mg/m^3 (ceiling limit) during the intermittent acid unloading process. The use of a dual diaphram pump (instead of compressed air) facilitated transfer of the acid up to the roof storage tanks and reduced the amount of acid released (especially at the completion of the unloading process) when compared to the use of compressed air. The installation of a wet scrubber (instead of direct venting) on all acid storage tank vents sharply reduced the acid mist released to the atmosphere.

2. Follow-up Evaluation, August 6-7, 1986

Predominant fungal species from the single and two-stage samplers, listed in decreasing order of airborne concentration, fell into five common environmental mold genera: Cladosporium, Penicillium, Fusarium, Alternaria, and Aspergillus. The lowest total fungal count (169 CFU/m^3) was obtained in the former stack maintenance room, reflecting the low activity level in this area. The pasteurization room, where stack maintenance work was currently being performed, had the highest fungal counts (507 to 1,746 CFU/m^3) over the two days of sampling. Figure 7 and Table 2 show the results of this sampling.

Although fungi were found growing on both plates of the Anderson two-stage samplers, the majority of fungal growth (74%) was counted on the second stage. This suggests that the majority of fungal particulates are in the respirable size range (capable of penetrating to the lower regions of the human respiratory tract). The lower percentage of non-respirable fungal particles may be due to the absence of gross airborne particle generation. Fungal counts also decreased in 50% of the 15-minute, two-stage

samples when compared to the 5-minute, two-stage samples begun at the same time and location. This decrease in fungal counts occurred in areas where higher fungal levels were anticipated. This may be due to the destruction of fungi (the vegetative cells) by trauma, or from clumping or overgrowth of the cells. Trauma, in this situation, may result from the mechanical shock of impact with the collection medium or, more likely, from dessication of the cells due to more air passing across the medium.

When using the N-6 modified Anderson samplers, fungal levels outside the plant exceeded the concentrations measured at each of the three sampling areas inside the plant. This discrepancy with the results from the two-stage samplers (which suggest the highest fungal counts were in the pasteurization room) may have occurred because air samples were collected over two consecutive days. Because sampling using the N-6 samplers was performed on different days, interpretation of the data is more difficult. These results underscore the variability in outdoor mold levels, which in turn may affect indoor levels.

Predominant bacterial and thermophilic actinomycetes identified by both the N-6 and 2-stage samplers were Bacillus, Streptomyces (grey/powdery and flat/wrinkled appearance), and Thermomonospora (yellow/wrinkled appearance). Although some media plates were too numerous to count reliably (predominantly overgrown with Bacillus), the majority of the thermophilic organisms identified had very low colony counts (ranging from 1 to 10 colonies) and have not been reported in the literature as principal causes of HP. These results are shown in Table 3.

Evaluation criteria for acceptable exposure to microbiological aerosols have not been formulated by NIOSH or OSHA because of the variability in outdoor microbiological levels and because many human factors, including genetic variability, determine whether a given airborne microbiological level will result in allergic illnesses, such as hypersensitivity pneumonitis. It should also be noted that bias in this type of study is towards lower total colony counts than may actually exist in the air. Counts of lightly inoculated media plates at later dates indicated total CFU's of heavy growth plates were 20-25% higher than indicated.

3. Follow-up Visit, December 3, 1986

On December 3, 1986 air samples were again collected for three classes of microorganisms: fungi, thermophilic actinomycetes, and bacteria. In this evaluation, area air samples were collected before, during, and after the electrodialysis stack cleaning process (still performed in the pasteurization room). Samples were collected with Anderson 2-stage viable samplers using a sample time of 5 minutes. Sample locations were in the pasteurization room and outside the plant. No samples were collected using the N-6 sampler. The results of the fungi and actinomycetes/bacteria sampling are shown in Figure 8 and Table 4.

The predominant fungal bioburden, listed in decreasing order of airborne concentration, were: Yeast, Cladosporium, Penicillium, and Aspergillus. Total viable counts (CFU/m^3) ranged from 106 (prior to electrodialysis stack maintenance) to 423 (during stack maintenance).

Concentrations of bacteria and thermophilic actinomycetes measured in the December 6 survey ranged from 282 to 3,211 CFU/m^3. The predominant species were Micrococcus, Streptomyces, and Bacillus, and concentrations of these three species increased markedly as electrodialysis stack maintenance was performed. For example, Micrococcus concentrations increased from 155 CFU/m^3 (prior to stack maintenance) to 3,211 CFU/m^3 during stack maintenance. Similar increases occured with Streptomyces and Bacillus.

B. Medical

1. Questionnaire Surveys

An initial medical questionnaire was self-administered to 75 workers on August 3-4, 1986. Eight delivery drivers and waste treatment operators, who worked in a building 200 yards away, were not asked to participate. Two workers refused to give blood. One of these workers completed the questionnaire, but was not asked to give blood because she believed she was pregnant. (This worker was not included in the analysis, although she reported a number of symptoms beginning in February 1985, 6 months before the other illnesses developed, and reported no exposure to ED membranes.) One worker gave blood but did not return the questionnaire. Six other workers were not available because of vacations or irregular, part-time work schedules.

The second questionnaire was administered on December 3-4, 1986. Fifteen of the original participants were not available, either because they were laid off, on vacation, or part-time workers. Of these, nine workers, including two who were laid-off, completed the questionnaire by telephone. Six participants were lost to follow-up despite numerous telephone calls, four were laid-off, and two were consistently unavailable. Therefore, the second questionnaire was completed by 69 (92%) of the original 75 study participants.

The questionnaire administered to 75 employees in August 1986, identified seven (9%) respondents as cases (four or more symptoms compatible with HP), and 61 (82%) non-cases, reporting one or fewer symptoms. Six workers reported two or three symptoms and were excluded from the remainder of the analysis. Among the seven cases were the four workers previously diagnosed with HP and the one worker diagnosed with asthma. One of the two other workers identified by the questionnaire as having symptoms compatible with HP had replaced one of the ill stack maintenance workers and reported symptoms compatible with HP in late December 1986 but was not evaluated medically until June 1987, when most symptoms had improved. Ultimately, the diagnosis of HP for this individual could not be confirmed. The other worker reported only one episode of illness after cleaning the membranes. This worker was interviewed and cautioned about a reoccurrence of the symptoms, but no further medical information was obtained.

Cases were significantly younger than non-cases, 32 vs 37 mean years of age (Table 5). (Three non-cases inaccurately listed their date of birth and were excluded from the age calculation.) Cases were less likely to report exposures to one or more hobbies capable of causing respiratory symptoms, such as working with hay, wood dust, or solvents. Only one case reported ever smoking cigarettes; none of the cases were current smokers.

Cases were more likely to report cleaning ED membranes than non-cases (Table 5). Two of the seven did this job for less than six months, and only one did it for more than four years. Six of the seven cases had cleaned ED membranes only in 1985 or 1986, as did 15 of the 20 non-cases who had ever cleaned the membranes.

2. Serology Results

The sera from 74 workers were tested for precipitins to 22 antigens, including samples of stack deposits, dust, milk and whey protein, and Thermophile and Penicillium sp. The prevalence of IgG precipitins to individual antigen samples varied from 100% to zero as shown in Table 6. The prevalence of precipitins to Aspergillus fumigatus (100%) and Bacillus sp. (80%) was unusually high. When 10 of the Aspergillus precipitins were randomly selected and tested for nonspecific "C" reactive

protein binding, none of the precipitin bands dissolved. Still, a control serum from one of the investigators was also positive for Aspergillus fumigatus and Bacillus sp., suggesting that nonspecific binding was responsible for the presence of precipitins in these two antigen extracts. For this reason, these two antigens were excluded from the remaining analysis.

Precipitins to yeast species (antigens three and four, see Table 1), were found in 13 (18%) of the samples. Five (7%) of the samples had precipitins to an antigen extract prepared from a mixture of four mold species (antigen 22). Five participants had precipitins to whey produced at the Monett plant, whereas only two had precipitins to whey supplied from a nearby Mid-America Dairymen plant located in Mt. Vernon, Missouri. Two workers had precipitins to Geotrichum sp.

Precipitins to yeast or whey proteins were not related to case status. Only one of the cases had precipitins to whey proteins, and only two had precipitins to yeast. Cases, however, were significantly more likely to have precipitins to at least one antigen, and to two or more antigens (Table 7). The odds ratio for three or more antigens was also high, although the 95% confidence interval included one. The two cases with multiple precipitins were among the first three stack maintenance workers to be diagnosed with HP. The last worker to be diagnosed with HP, in March 1986, had no precipitins. Of the four workers diagnosed with HP, only two had precipitins. The presence of precipitins was not associated with exposure to ED membranes (Table 8).

3. Other Studies

In August 1985 the percent of ED stacks recorded on maintenance log sheets as "dirty" (heavier than usual accumulations of protein and mineral deposits on the membranes), shown in Figure 5, markedly increased. Because the log was maintained by the same two workers, the increase, which began in August, 1986 before the workers became ill, is not likely to be a surveillance artifact. After the first three workers went on medical leave, however, the log was no longer maintained. Still, anecdotal reports by employees suggest that the increase in "dirty" stacks lasted until February or March, 1986. During our plant visits in May, August, and December 1986, no deposits were noticeable on the membranes. No changes that may have reduced the quantity of membrane deposits could be identified in the operating or cleaning system.

Review of company cheese yield records identified a peak seasonal fluctuation during the fall season. The peak occurred after illnesses first began. This seasonal fluctuation in cheese yield is reported by the company to be a function of the cows' lactation status.

Cultures of whey samples identified numerous yeast species. A heavy growth of Geotrichium sp. and Candida sp. were identified from the stack deposit cultures. Although not identified in air samples, Penicillium roqueforti quickly overgrew cheese curd samples that were collected at the plant and allowed to spoil in a sterile container at room temperature.

Review of climatological data identified an unusually high level of precipitation (12 inches) for the Springfield, Missouri area in November 1985. This level was the second highest level ever recorded in the city and 300 percent above the 20-year average for that month. Beginning in August 1985, the number of cloudy days recorded was also above normal when compared to the 20-year average. These data are shown in Figure 6.

Medical studies of three current stack maintenance workers conducted in December 1986 revealed no relevant abnormalities.

VII. DISCUSSION

A. Microbiological Sampling

In general, the microbiological sampling results showed a trend of increasing airborne mold level with increasing activity level. The stack maintenance room showed the lowest fungal levels, but the room was seldomed used at the time of this investigation. Higher airborne fungal levels were found in the pasteurization room, where ED stack maintenance was currently performed. Microorganism concentrations in the pasteurization room, in general, were also higher than those measured in the whey separation room. These higher levels reflect air movement and organic aerosols generated from the ED stack cleaning technique in use during this evaluation. Although high-powered water sprays are employed in the whey separation room, they are used to wash down the floor and not to clean organic deposits from ionic membranes.

One conclusion from the data is that cleaning ED stack membranes temporarily increases levels of airborne microorganisms relative to other areas of the plant. Levels of microrganisms collected after ED membrane cleaning had begun were twice the levels collected prior to cleaning (increases in yeast and bacterial species were most notable). Presumably non-viable airborne particles (dead microbiological organisms and whey proteins) are also increased in a similar fashion. As noted earlier in this report, deposits on uncleaned membrane stacks provide a good culture medium for fungi, yeast, and bacteria.

B. Questionnaire Survey

The high attack rate of respiratory illness in stack maintenance workers in November 1985 (75%) quickly focused management attention on assessing the ventilation in the small 200 square foot stack maintenance room. A poorly maintained ventilation system may have exacerbated antigen exposure for the first three workers who became ill. Steam cleaning the fan coil unit, and moving the process to a larger, better ventilated, room were appropriate short-term responses. When a fourth stack maintenance worker became ill, attention was focused on the process itself and not on the malfunctioning air handling unit as the cause of illness.

Of the seven workers identified through the questionnaire with symptoms compatible with HP, timely medical data were available for only five. Four workers had been diagnosed with HP and one with asthma. Another reported symptoms compatible with HP but was not evaluated medically until symptoms had improved, and the diagnosis of HP could not be clinically confirmed. The seventh worker reported one episode of illness after working with the membranes in March 1986, and reported no subsequent exposures or episodes of illness. No further medical data were available on this worker.

C. Serology Results and Hypersensitivity Pneumonitis

Penicillium roqueforti, previously reported as an etiologic agent in cheese workers' HP,[1] was cultured from bulk cheese curd samples, but not from airborne samples. Heavy accumulations of stack deposits, reported by employees during the fall of 1985, could have allowed overgrowth of this natural cheese contaminant. Subsequent membrane washing with a high powered water spray could have aerosolized particles of this and other fungi. After years of low-level exposure to aerosolized stack deposit particles, workers were exposed to much higher levels. The hypothesis that this precipitated the onset of illness is supported by current knowledge about the development of HP. Both duration and dose of exposure to an antigen are determinants in development of HP.[21]

However, none of the serum samples collected by NIOSH investigators in August 1986 tested positive for precipitins to Penicillium species. Not even the four workers clinically diagnosed with HP had precipitins to Penicillium species, although three did in tests conducted by their private physician in December 1985.

Possible explanations for the difference in serological results in the workers diagnosed with HP between the fall of 1985 and the fall of 1986 are: (1) antibody levels had declined between peak exposures in 1985 and the date of sampling in August 1986; (2) tests for precipitins conducted in December 1985 used different antigens and preparation techniques (including the use of dimethyl sulfoxide); and (3) the test used in August 1986, the exoantigen test, although useful for screening precipitins to a large number of antigens, is not sensitive to low levels of antibody.

No association was identified between the marker for antigen exposure (precipitins) and cleaning stack membranes. If cleaning ED membranes were the only source of aerosolized antigens, and if precipitins are a biological marker for exposure to these antigens, workers with exposure to the membranes should have developed precipitins.

The ability of this study to identify an association between the marker for exposure (precipitins) and the hypothesized exposure (cleaning ED membranes) is determined by: (1) biological factors that determine whether an immune response (precipitins) will develop, and (2) study design factors (improper classification of worker exposure) that affect the ability to identify an association.

Two biological factors could have obscured an association: (1) low levels of aerosolized antigens may have been widely dispersed throughout the plant, stimulating the development of antibodies in susceptible workers throughout the plant, and (2) many workers reported short-term exposure to the membranes and may not have developed a measurable antibody response.

Four study design factors could have obscured an association. (1) "Exposure" to ED membranes was broadly defined as "ever" having worked cleaning the ED mebranes and included stack workers who washed the outside of stacks but did not disassemble and hand-clean the membranes. (2) The appropriate antigen may not have been tested. (3) Double diffusion tests do not identify precipitins present at low levels. (4) The worker with symptoms compatible with HP, but diagnosed with asthma, was not excluded from the analysis.

The observation that smoking appeared to be inversely associated with reporting symptoms compatible with HP may be related to the effect of smoke, or its constituents, on the immune system. Increased respiratory secretions in smokers may block development of an immune response by preventing deposition of small particles in the lung.[22] Smoke may directly interfere with development of an immune response in the alveoli.[23]

D. Electrodialysis Stack Maintenance Ventilation

The engineering controls described should greatly decrease the inhalation hazard by removal of the proteinaceous materials. A number of ventilation control alternatives were considered for control of aerosols generated in the stack maintenance procedure.[24] For a work bench that is approximately 4.5 by 4.5 feet, the alternatives were: (1) a backdraft multiple slot hood similar to a welding bench design; (2) a push-pull design consisting of a downdraft hood, located below the working surface, where capture is aided by air blowing from a 1/4 inch by 4 foot slot located 5 to 7 feet above the working surface; and (3) a booth in which air is uniformly supplied at the top and exhausted at its floor level.

The backdraft multiple-slot configuration has the disadvantage that the presence of the worker's body in front of the slots creates a wake (eddy currents) which is known to contribute significantly to exposure. Briefly, contaminants generated at the work station may be entrained into the two stationary vortices constituting the wake.

The push-pull system investigated consisted of an isothermal jet of air with a total flow of 83 cubic feet per

minute (cfm) per linear foot impinging on a downdraft exhaust hood with a flow of 2000 cfm from a height of 5 feet. A grating on the surface of the 4.5 by 4.5 foot downdraft hood would become the working surface. The jet velocity profile calculated for the case of the exhaust opening not obstructed by the ED stacks indicated a poor distribution of velocity across the width of the working surface. The calculations were made using models developed by Walker for a slot jet adjacent to a wall.[25]

A ventilation system which eliminates the drawbacks of both the backdraft and push-pull systems described above is shown in Figure 9. The configuration follows an extensively investigated spray booth used for painting cars.[26] "Blowing" configuration No. 2 and "exhaust" configuration No. 4 were selected. The average velocity for this configuration is 100 feet per minute (fpm). For one 4.5 by 4.5 ft work station the booth dimensions are approximately 8 ft wide and 7 ft deep, resulting in a average velocity of less than 160 fpm in the plane of the work station. The surface of the table should consist of a grating to facilitate the passage of air and water.

Good air distribution at the inlet and exhaust plenum are important for proper operation. Air may be recirculated if the proper amount of fresh outside air is introduced, and care is taken to dehumidify, condition, and filter the air supply. The air filter should be of the high efficiency type (i.e. 99.94% removal with respect to particles 0.3 u in diameter). A maximum of 35 cfm of outside fresh air per occupant should be allowed for a total of 200 cfm. Care should be taken in designing the system so that component cleaning is possible, preventing growth and accumulation of microorganisms.

VIII. CONCLUSIONS

There is a clear association in time and place between cleaning stacks of electrodialysis membranes and HP in the four workers previously diagnosed with the disease. Furthermore, the seven cases defined through the questionnaire were more likely to report exposure to ED stack membranes than were non-cases.

NIOSH investigators were unable to identify a specific agent or antigen responsible for illness in these workers. Stacks of ED membranes waiting to be cleaned can provide an ideal growth medium for microbiological species, as demostrated from the cultures of bulk samples. Since a marked increase in viable airborne microorganisms occurred during the cleaning process, it is likely that non-viable proteins are similarly increased. Greater numbers of aerosolized microorganisms were probably generated from August 1985 to March 1986, when visible stack deposits were noticed by the employees. Reasons for the increase in stack deposits are still undetermined, but may relate to seasonal changes in milk production, influences of unusual weather conditions, or as yet undetermined production factors.

Air samples for microorganisms collected in August and December 1986 may not represent exposure conditions during the previous fall and winter. For example, in addition to the nine months which elapsed from reports of employee illness to the collection of the first air samples, the ventilation system in the original stack maintenance room was removed and replaced and the ED membrane cleaning moved to a larger, better ventilated area. Also, the bioaerosol sampling conducted in this investigation would not account for non-viable proteinaceous material which may be generated during membrane cleaning.

It is not surprising that one antigen could not be associated with case status because precipitins to individual antigens are not well correlated with HP.[19,22] The presence of one or more antigens was, however, associated with case status, indicating either that illness may have resulted from exposure to multiple antigens or that exposure to multiple antigens was associated with exposure to a specific, unidentified antigen responsible for HP among the workers.

IX. RECOMMENDATIONS

1. Introduce engineering and work-practice changes to reduce aerosol generation and inhalation. Decrease use of high powered waterspray and, as discussed in Section VIII, improve ventilation in the stack maintenance room by providing fresh make-up air during the cleaning operation.

2. Develop a system to correlate changes in stack deposits with production and season variables.

3. Decrease time that stacks remain idle before being cleaned.

4. Provide periodic medical monitoring (symptom history, chest examination, pulmonary function tests) of full-time stack maintenance workers to detect early indications of respiratory disease.

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XII. DISTRIBUTION AND AVAILABILITY OF REPORT

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Publications Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days, the report will be available through the National Technical Information Service (NTIS), 5285 Port Royal, Springfield, Virginia 22161. Information regarding its availability through NTIS can be obtained from NIOSH Publications Office at the Cincinnati address. Copies of this report have been sent to:

1. Mid-America Dairymen, Inc., Springfield, Missouri
2. Mid-America Dairymen, Inc., Monett, Missouri
3. NIOSH, Denver Region
4. OSHA, Region VIII

For the purpose of informing affected employees, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calendar days.

TABLE 1

PANEL OF ANTIGENS USED TO TEST FOR PRECIPITINS

Mid-America Dairymen, Inc.,
Springfield, Missouri
HETA 86-273
August 30, 1986

1. Negative control V9 agar
2. Negative control TS agar
3. Bivalent yeasts
4. Bivalent yeasts
5. Vacuumed dust samples
6. Whey - Mt. Vernon, Missouri plant
7. Whey - Monett, Missouri plant
8. Stack deposit
9. Double cheese food coloring
10. Geotrichum sp.
11. Alternaria sp.
12. Fusarium sp.
13. Penicillium camemberti
14. Penicillium roqueforti
15. Penicillium casei
16. Penicillium sp. (mixed)
17. Aspergillus sp. (bivalent)
18. Aspergillus fumigatus
19. Thermophile (bivalent)
20. Thermophile (bivalent)
21. Cladosporium
22. Mold mix (quadravalent)
23. Streptomyses sp.
24. Bacillus sp.

Table 2
Concentrations of Airborne Fungi
Two-Stage Viable Air Samples, 5 and 15 Minute Sample Duration
Mid-America Dairymen, Inc.
Monett, Missouri
HETA 86-273
August 6-7, 1986

LOCATION	15 MINUTE SAMPLES		5 MINUTE SAMPLES	
	Total (CFU/m^3)[b]	Predominant Species[a] (CFU/m^3)	Total (CFU/m^3)	Predominant species (CFU/m^3)
Whey Separation Room	586	Cladosporium (180) Penicillium (26) Alternaria (20)	1,106	Penicillium (85) Cladosporium (48) Alternaria (12)
Pasteurization Room	607	Yeast (200) Penicillium (42) Cladosporium (25)	1,746	Cladosporium (176) Penicillium (63) Alternaria (4)
Former Stack Maintenance Room	428	Cladosporium (92) Penicillium (65) Geotrichum (16)	169	Cladosporium (10) Penicillium (7) Fusarium (4)
Outside	882	Cladosporium (230) Penicillium (82) Camarosporium (35)	748	Cladosporium (230) Penicillium (74) Aspergillus (8)

a. The three most abundant fungal species are listed by decreasing order of airborne concentration, with corresponding airborne concentrations in parenthesis.
b CFU/m^3 = colony-forming units per cubic meter of air. Total CFU's represents the sum of all colonies from both stages.

Table 3
Concentrations of Airborne Bacteria
Two-Stage and N-6 (Modified Single-Stage) Viable Air Samples[a]
Mid-America Dairymen, Inc.
Monett, Missouri
HETA 86-273

August 6-7, 1986

	15 MINUTE SAMPLES		5 MINUTE SAMPLES	
LOCATION	Species (No. of colonies)	Comments	Species (No. of colonies)	Comments
Whey Separation Room	Thermophilic Streptomyces (2)	Flat, wrinkled appearance	Thermophilic Bacteria (2)	Predominately Bacillus
			Thermophilic Bacteria	Too numerous to count
Stack Maintenance Room	Thermophilic Bacteria (18)	Predominately Bacillus		
	Thermophilic Streptomyces (2)	Flat, wrinkled appearance		
Pasteurization Room	Thermophilic Bacteria	Too numerous too count	Thermophilic Streptomyces (3)	Grey, powdery appearance
			Thermomonospora sp. (1)	Yellow, wrinkled appearance
			Thermophilic Streptomyces (1)	Flat, wrinkled appearance

continued

Table 3 (continued)
Concentrations of Airborne Bacteria
Two-Stage and N-6 (Modified Single-Stage) Viable Air Samples[a]

Mid-America Dairymen, Inc.
Monett, Missouri
HETA 86-273

August 6-7, 1986

LOCATION	15 MINUTE SAMPLES Species	15 MINUTE SAMPLES Comments (No. of colonies)	5 MINUTE SAMPLES Species	5 MINUTE SAMPLES Comments (No. of colonies)
Outside	Thermophilic Bacteria	Too numerous too count	Thermophilic Bacteria (3)	Predominately Bacillus
	Thermophilic Streptomyces (1)	Grey, powdery appearance	Thermophilic Streptomyces (1)	Grey, powdery appearance
			Thermophilic Bacteria	Too numerous too count
			Thermomonospora sp.	Yellow, wrinkled appearance

a Five and fifteen minute samples were collected with the two-stage viable air sampler. Only 5 minute samples were collected with the NIOSH modified single-stage sampler.

Comment: None of the thermophilic actinomycetes isolated from this group of samples are reported in the literature as principal causes of hypersensitivity pneumonitis.

Table 4
Concentrations of Airborne Fungi, Bacteria, and Thermophilic Actinomycetes
Two-Stage Viable Air Samples, 5 Minute Sample Duration
Pasteurization Room
Mid-America Dairymen, Inc.
Monett, Missouri
HETA 86-273

December 3, 1986

	FUNGI		BACTERIA/THERMOPHILIC ACTINOMYCETES	
ACTIVITY	Total (CFU/m^3)	Predominant Species(CFU/m^3)[a]	Total (CFU/m^3)	Predominant species(CFU/m^3)[a]
No Stack Maintenance	148	Cladosporium (63) Yeast (21) Aspergillus (21)	282	Micrococcus (155) Bacillus (85) Streptomyces (42)
	106	Penicillium (70) Cladosporium (35)		
	134	Cladosporium (56) Non-sporulating (35) Penicillium (21)		
Start of Stack Cleaning	401	Yeast (254) Cladosporium (78) Aspergillus (35)		
During Stack Cleaning	423	Yeast (303) Cladosporium (56) Penicillium (35)	3,211[b]	Micrococcus (2,851+) Streptomyces (366) Bacillus (282)
After Stack Cleaning			401	Micrococcus (211) Streptomyces (127) Bacillus (63)

a CFU/m^3 = colony-forming units per cubic meter of air. Total represents the combined sum of colonies from both stages.
b The three most abundant fungal species are listed by decreasing order of airborne concentration, with corresponding airborne concentrations in parenthesis.
c Plate counted after 2 days. Micrococcus count is estimated due to overgrowth.
General Comments: Culture plates were counted following 3 days of incubation (unless otherwise noted).

TABLE 5

COMPARISON OF DEMOGRAPHIC AND EXPOSURE VARIABLES BY CASE STATUS

Mid-America Dairymen, Inc.,
Springfield, Missouri
HETA 86-273

August 30, 1986

DICHOTOMOUS VARIABLES	CASES WITH VARIABLE	NON-CASES WITH WITH VARIABLE	ODDS RATIO	95% CONFIDENCE INTERVAL
NUMBER OF PARTICIPANTS	7	61		
EDUCATION (post H.S.)	2	24	0.62	0.05, 4.18
MEDICAL (one or more current or previous problems)	3	20	1.10	0.15, 7.04
FAMILY HISTORY OF ALLERGY	0	a	0	0.00, 3.72
CURRENT SMOKER	0	19	0	0.00, 1.72
EVER SMOKED	1	37	0.11	0.00, 1.01
OWN PETS	4	42	0.68	0.09, 4.56
EVER LIVE ON FARM	5	54	0.32	0.04, 4.10
HOBBY	1	38	0.10	0.00, 0.94
HAY	1	29	0.18	0.00, 1.69
PAINT, SOLVENTS	1	17	0.43	0.01, 4.02
WOOD DUST	0	20	0	0.00, 1.59
PREVIOUS JOB (one or more exposures)	3	41	0.37	0.05, 2.43

continued

TABLE 5 (continued)

COMPARISON OF DEMOGRAPHIC AND EXPOSURE VARIABLES BY CASE STATUS

Mid-America Dairymen, Inc.,
Springfield, Missouri
HETA 86-273

August 30, 1986

DICHOTOMOUS VARIABLES	CASES WITH VARIABLE	NON-CASES WITH WITH VARIABLE	ODDS RATIO	95% CONFIDENCE INTERVAL
WHEAT, GRAIN	1	23	0.28	0.01, 2.54
EVER WORKED CLEANING ED MEMBRANES	7	20[b]	Undefined, p=0.0014[c]	
CONTINUOUS VARIABLES	MEAN, NUMBER, STANDARD ERROR OF MEAN t VALUE	MEAN, NUMBER STANDARD ERROR OF MEAN P VALUE		
AGE	32, 7, 1.99	37, 58, 1.52	2.34	0.034
LENGTH OF EMPLOYMENT	7.4, 7, 1.20	9.9, 60, 1.00	1.59	0.129
YEARS ON FARM	25, 4, 2.88	20, 53, 1.94	0.65	0.519
COLDS (per year)	1.6, 7, 0.29	1.7, 55, 0.23	0.13	0.899

a Information available for only 55 non-cases.
b Information available for only 57 non-cases.
c Fisher's exact test, 2-tailed.

TABLE 6

PREVALENCE OF IgG PRECIPITINS
AMONG 74 PARTICIPANTS

Mid-America Dairymen, Inc.,
Springfield, Missouri
HETA 86-273

August 30, 1986

	ANTIGEN *	PERCENT POSITIVE
1.	Yeast Sp.	17
2.	Whey proteins	18
3.	Mold Mix	7
4.	Geotrichium Sp.	3
5.	Dust Sample	1
6.	Stack Deposit	1
7.	Whey sample	1
8.	Thermophile sp.	1
9.	Bacillus sp.	80
10.	Aspergillus fumigatus	100

* No participant had IgG precipitins to the other antigens, including Penicillium sp. (Table 1).

TABLE 7

COMPARISON OF PRECIPITINS BY CASE STATUS

Mid-America Dairymen, Inc.,
Springfield, Missouri
HETA 86-273
August 30, 1986

POSITIVE PRECIPITINS	CASES WITH VARIABLE	NON-CASES WITH VARIABLE	ODDS RATIO	95% CONFIDENCE INTERVAL
Number of participants	7	61		
One or more	7	15	Undefined	R=0.0002[a]
Two or more	4	4	19.0	2.17, 167
Three or more	2	1	24.0	0.97, 143
Precipitins to individual agents:				
Yeast	2	11	1.8	0.15, 12.9
Whey Proteins	1	4	2.4	0.04, 29.6

a Fisher's exact test, 2-tailed.

TABLE 8

PRESENCE OF PRECIPITINS BY
HISTORY OF ELECTRODIALYSIS MEMBRANE EXPOSURE

Mid-America Dairymen, Inc.,
Springfield, Missouri
HETA 86-273
August 30, 1986

	EXPOSURE PRESENT	EXPOSURE ABSENT	RELATIVE RISK	(95% CONFIDENCE INTERVAL)
Number of participants	31	38		
Number of precipitins present				
≥ 1	6 (19)[a]	9 (24)	0.82	0.33, 2.05
≥ 2	2 (6)	3 (8)	0.82	0.15, 4.59
≥ 3	2 (6)	1 (3)	2.45	0.23, 25.8

a Number and (percent) of participants.

FIGURE 1
Plant Schematic

Mid-America Dairymen, Inc.
Springfield, Missouri
HETA 86-273

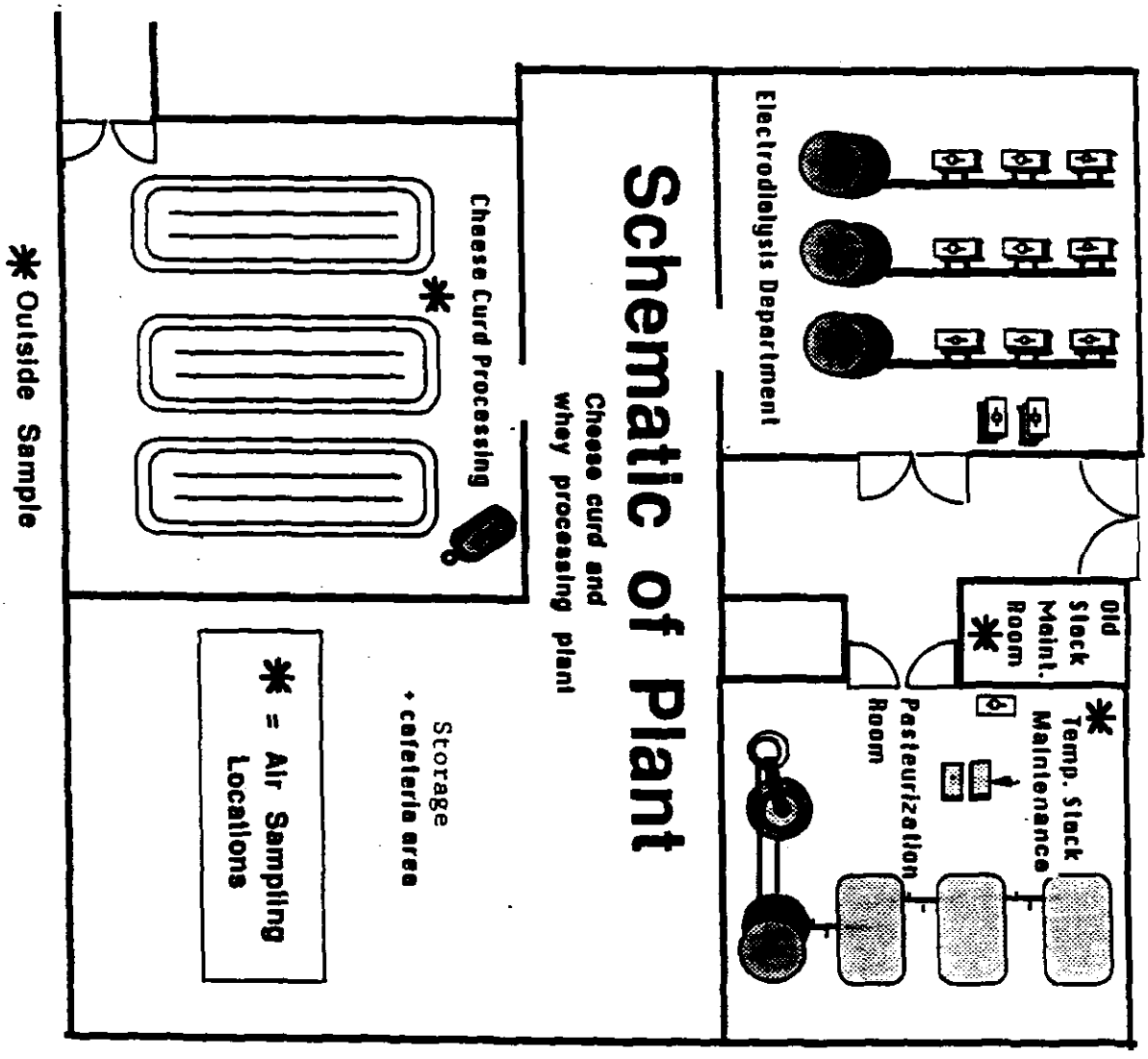


FIGURE 2

"Tortuous Path" Electrodialysis Membrane

Mid-America Dairymen, Inc.
Springfield, Missouri
HETA 86-273

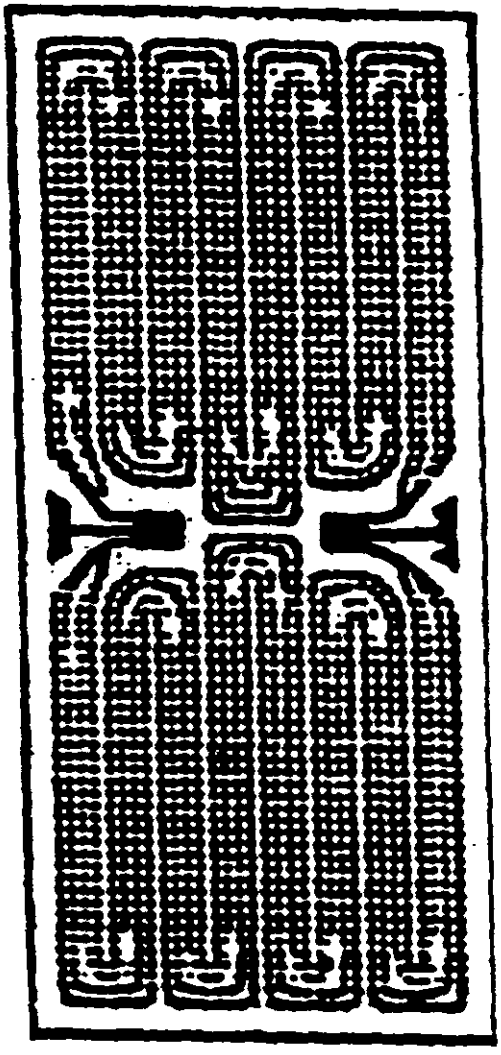


FIGURE 3
Diagram of a Typical Fan Coil Ventilation Unit

Mid-America Dairymen, Inc.
Springfield, Missouri
HETA 86-273

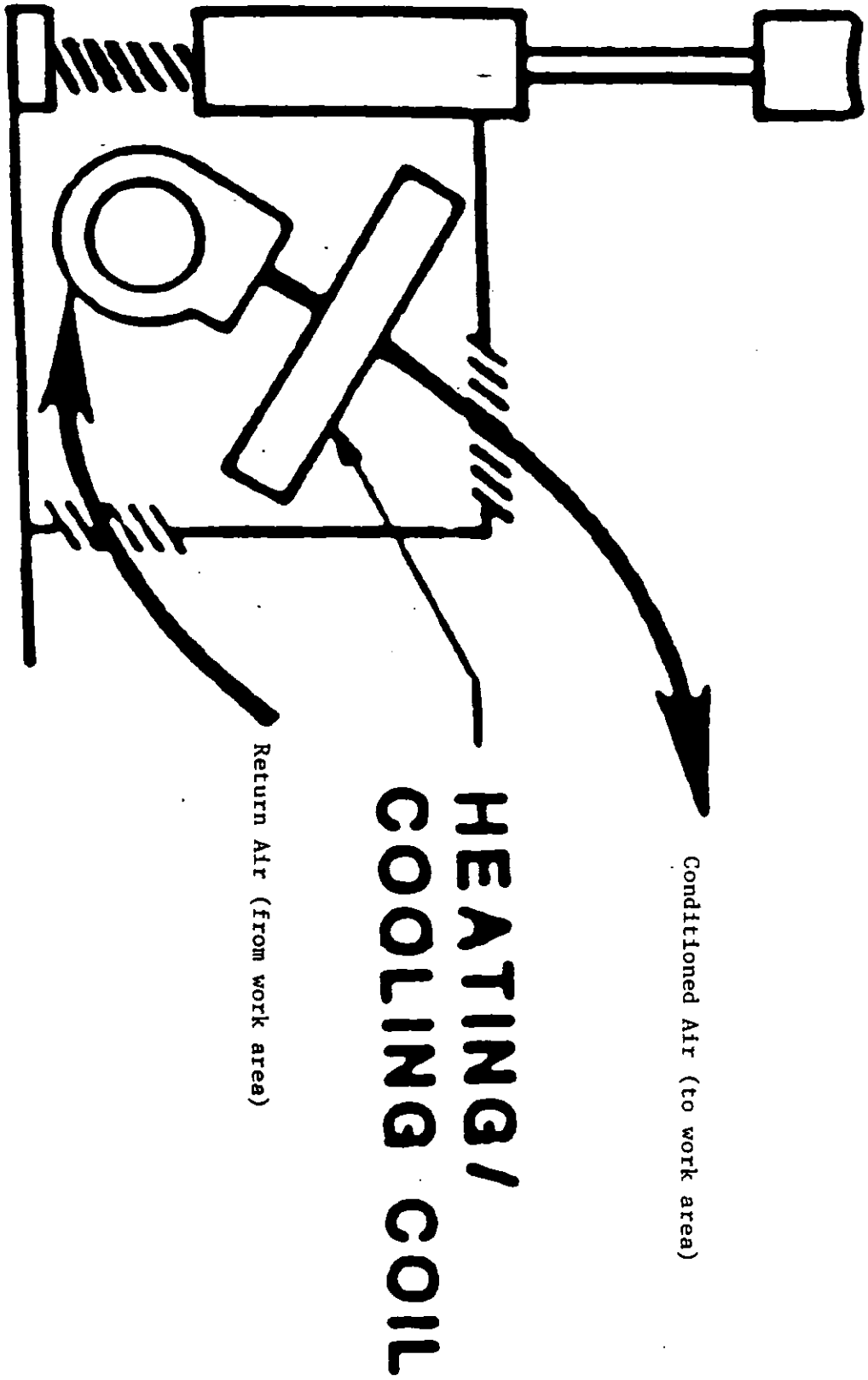
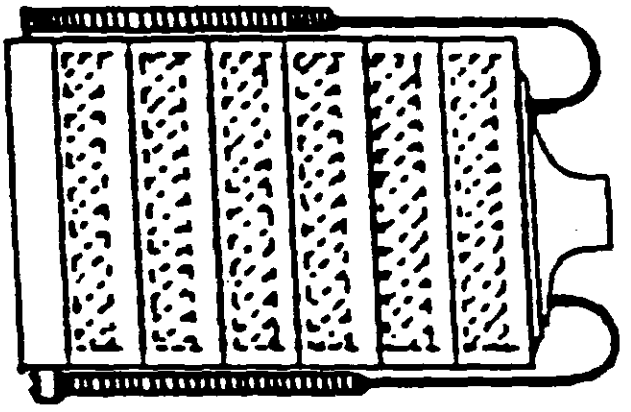


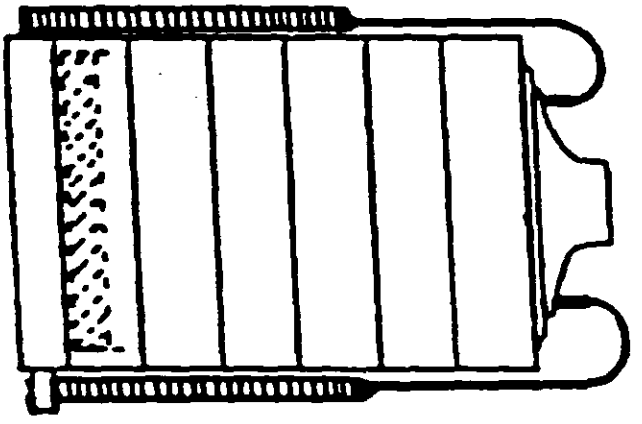
FIGURE 4
Examples of Viable Air Samplers

Mid-America Dairymen, Inc.
Springfield, Missouri
HETA 86-273



STANDARD ANDERSEN

Six media plates



S_6

Only sixth media plate is used.

N_6

NIOSH modified Anderson Six Stage Sampler. Only the sixth stage and one media plate is used.

FIGURE 5

Percentage of "Dirty" Membranes Reported by Employees

Mid-America Dairymen, Inc.
Springfield, Missouri
HETA 86-273

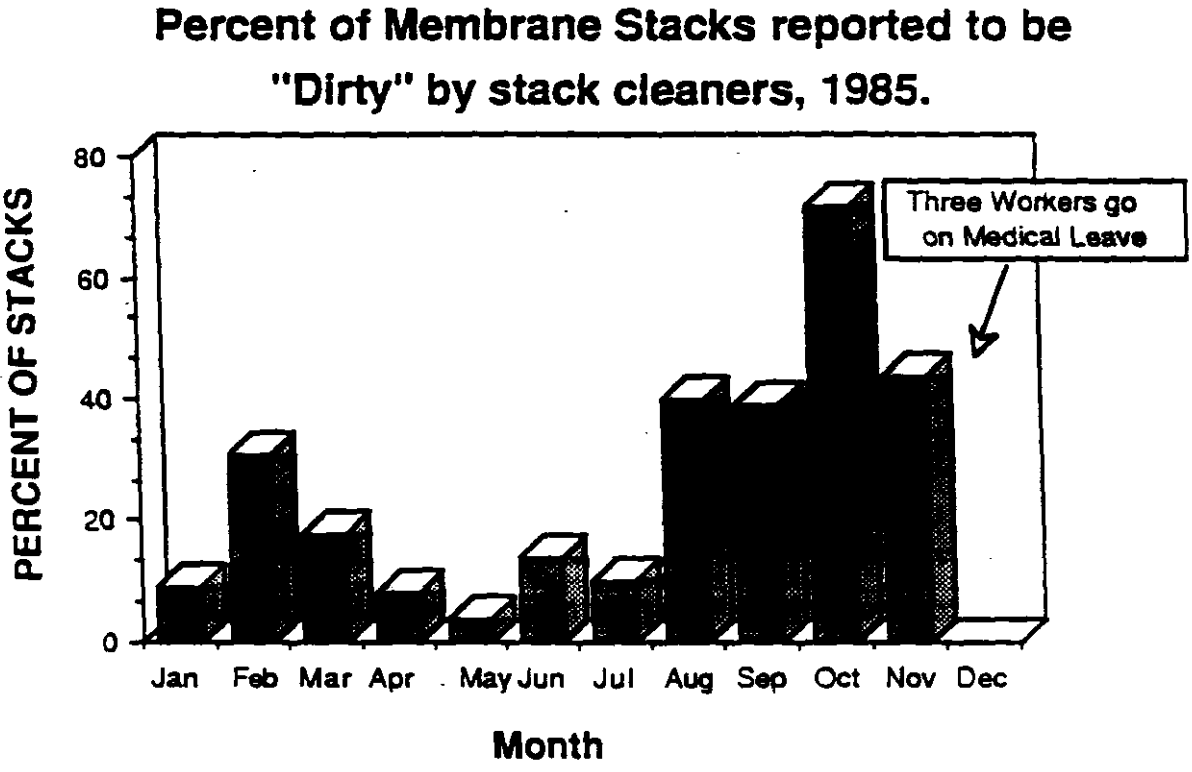
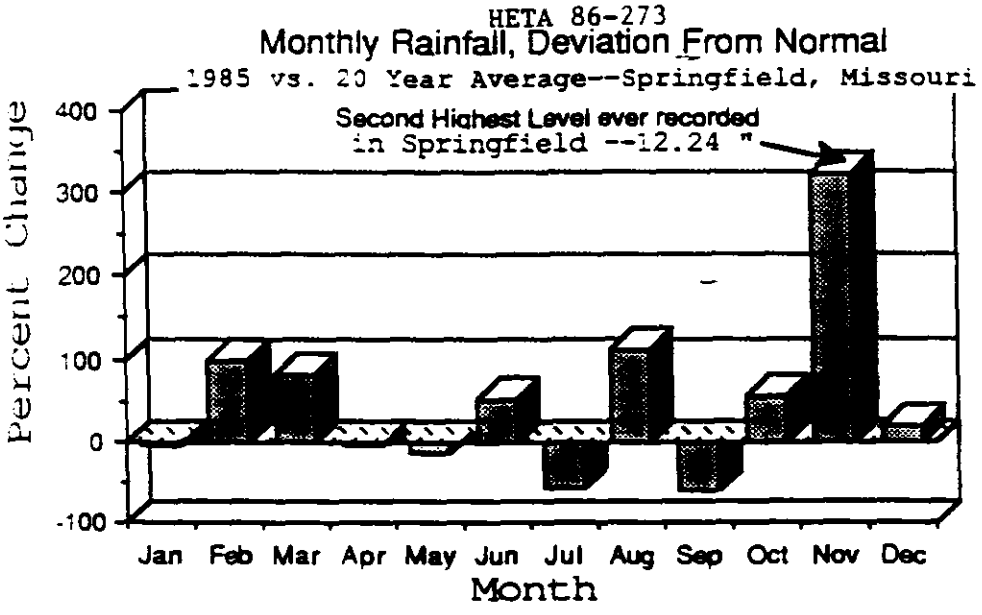
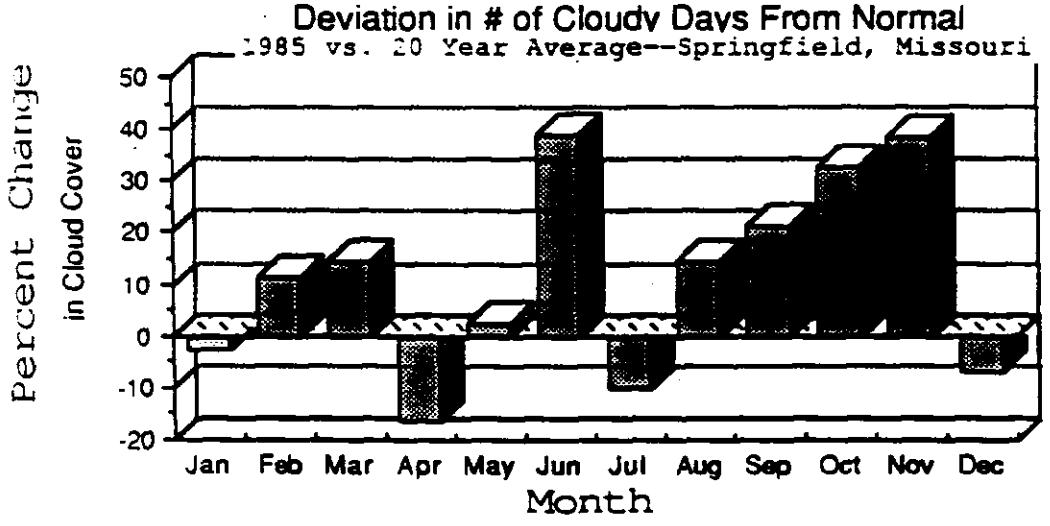


FIGURE 6
Climatological Data - 1985 and 1986

Mid-America Dairymen, Inc
HETA 86-273





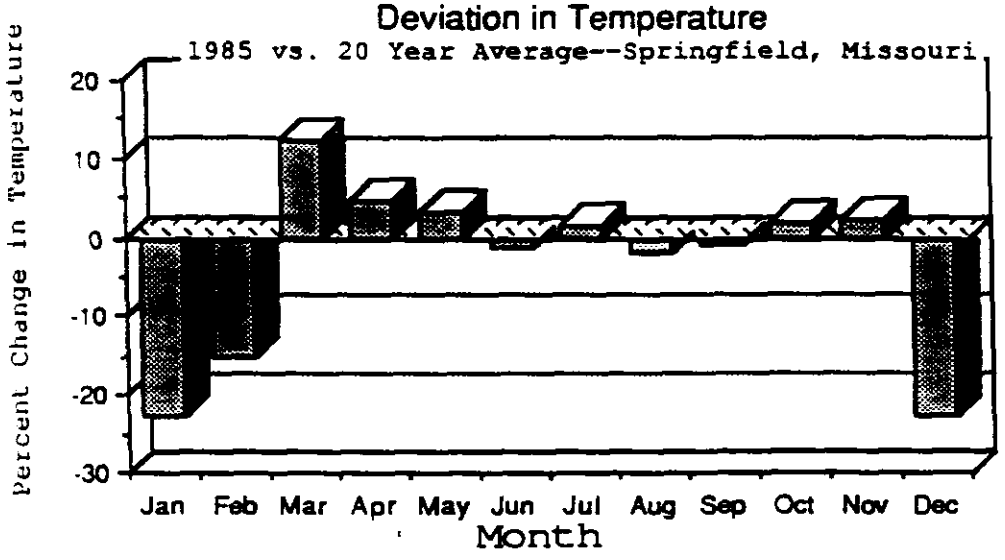
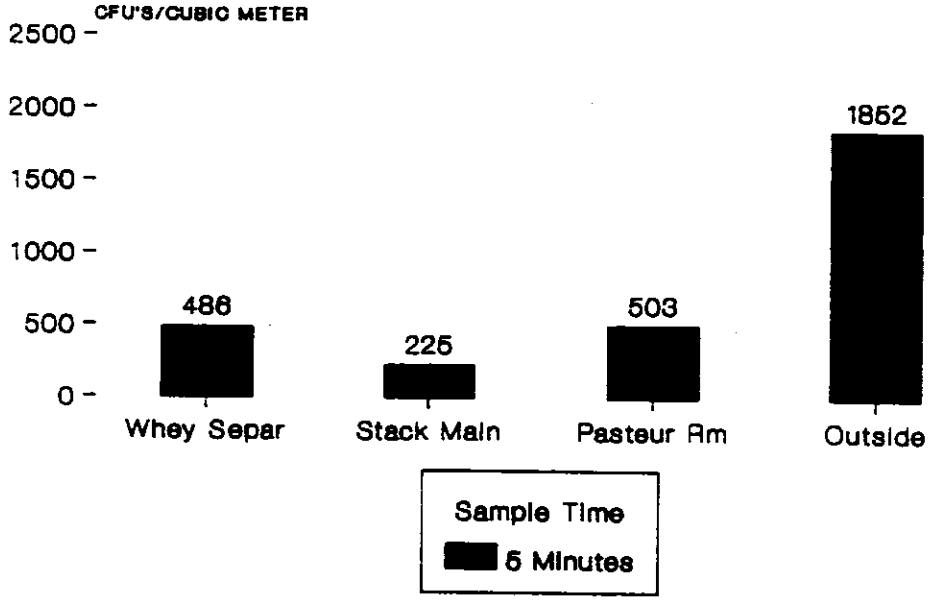


FIGURE 7

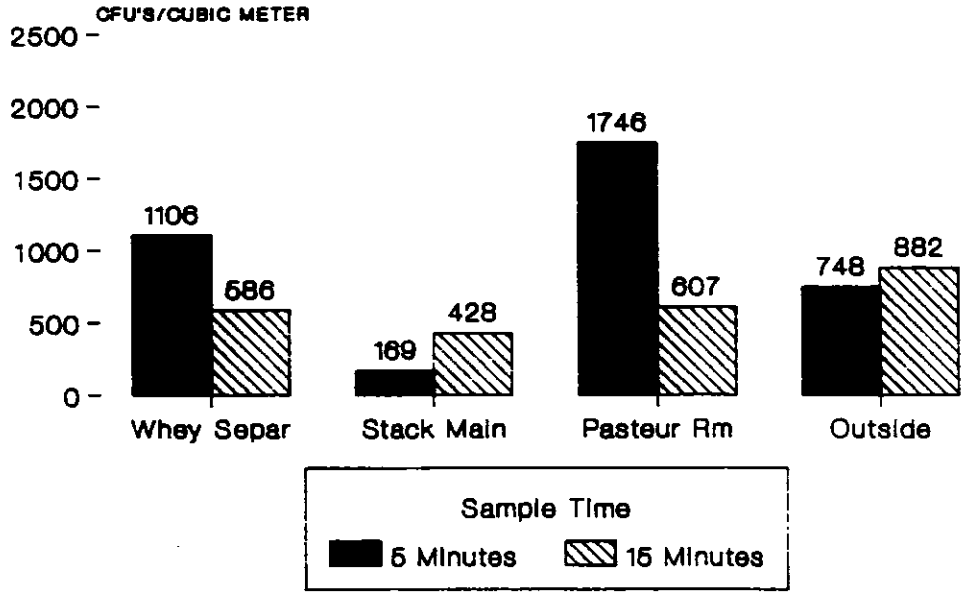
Mid-America Dairymen, Inc.
Springfield. Missouri
HETA 86-273

VIABLE AIR SAMPLES-FUNGI
ONE-STAGE SAMPLER (TOTAL COUNT)



August 6-7, 1986
Media: V-9 Agar
CFU - Colony Forming Units

VIABLE AIR SAMPLES-FUNGI
TWO-STAGE SAMPLER (TOTAL COUNT)

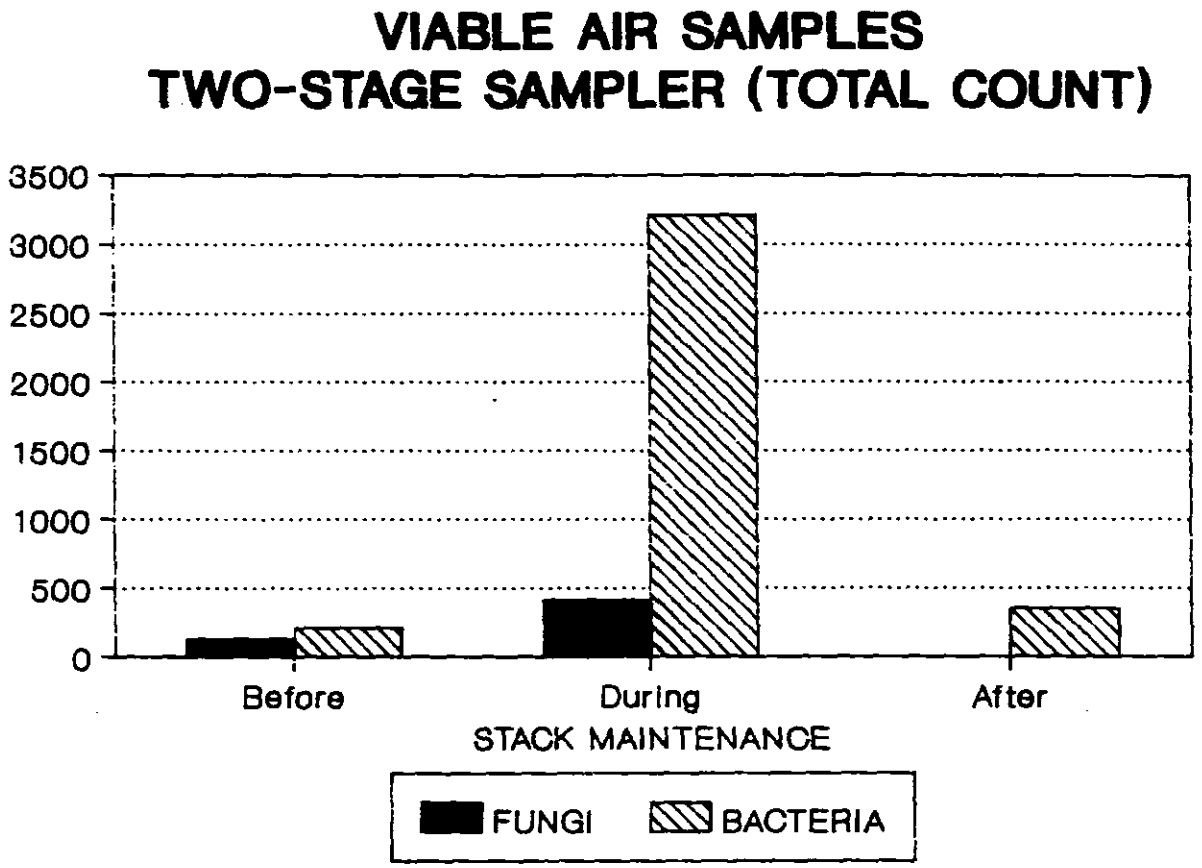


August 6-7, 1986
Media: V-9 Agar
CFU - Colony Forming Units

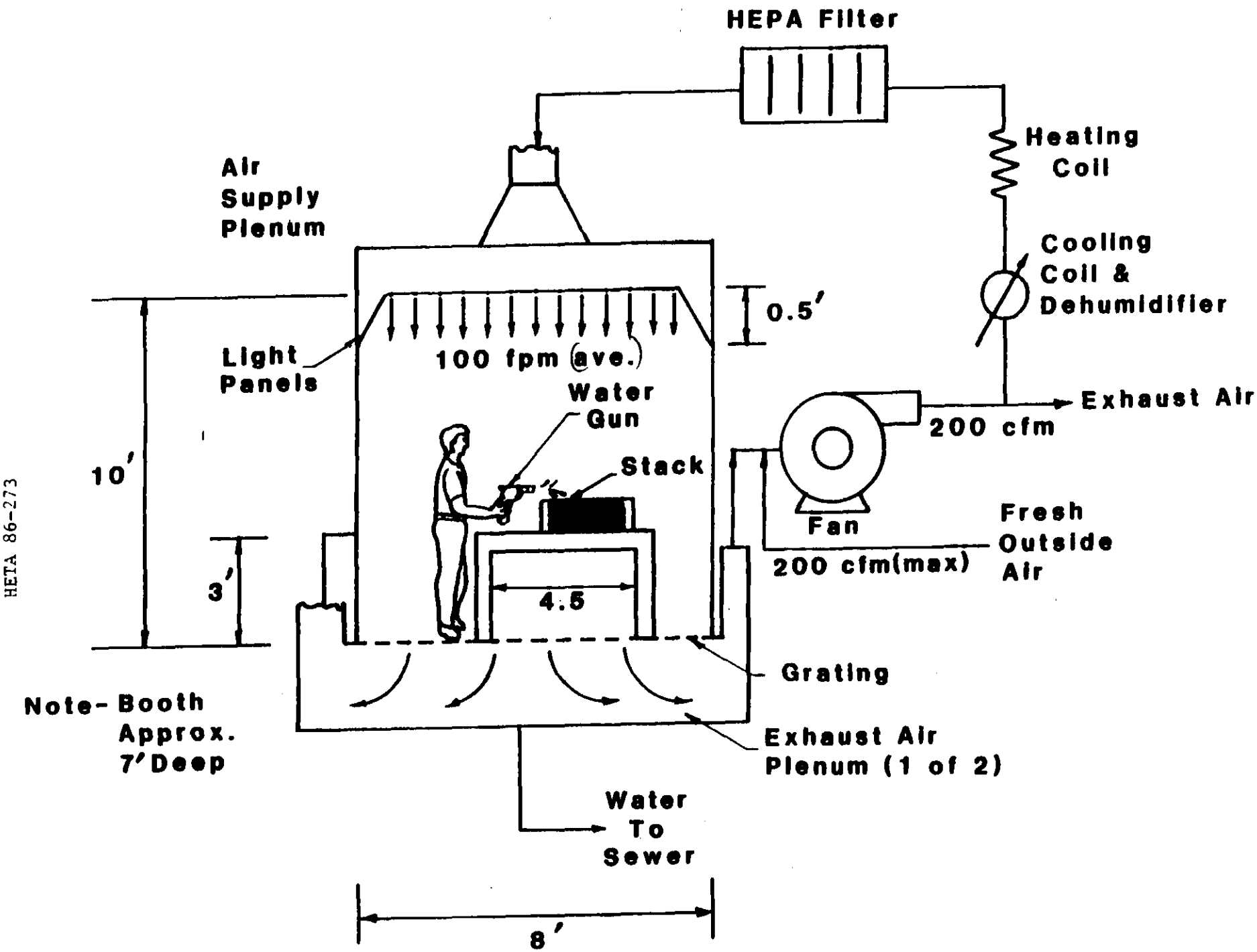
FIGURE 8

Two-Stage Viable Air Sampling for Fungi
and Bacteria

Mid-America Dairymen, Inc.
Monett, Missouri
HETA 86-273



December 3, 1986 Sample time 5 minutes
Media: V-8 Agar (Fungi) TSA (Bacteria)
No fungi sample collected after cleaning



Mid-America Dairymen, Inc.
Springfield, Missouri
HETA 86-273

Fig. 9 .Booth for Stack Maintenance