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I. SUMMARY

On September 14, 1992, the National Institute for Occupational Safety and Health (NIOSH) received a report of 31 cases of green tobacco sickness (GTS) in tobacco harvesters who sought treatment in several south-central Kentucky hospital emergency departments. The report was made by an occupational nurse in Bowling Green, Kentucky who worked with the Occupational Health Nurses in Agricultural Communities (OHNAC) Project of Kentucky. A team from NIOSH traveled on September 15 to the two areas in Kentucky from where the reports originated, to review the medical records of the ill workers and to initiate a medical records search in local hospitals.

The State Epidemiologist for the state of Kentucky requested technical assistance from NIOSH on September 21 to investigate the reported cases of green tobacco sickness. On September 25, an industrial hygiene team observed work practices of tobacco harvesting at two farms; one in Kentucky and one in Ohio. On September 28, investigators from NIOSH and Kentucky-based occupational health nurses initiated a case-control study in order to evaluate possible risk factors for the condition.

There are approximately 60,000 full- and part-time tobacco harvesters in Kentucky, and an estimated 4730 tobacco harvest workers in the five counties from which the reports originated.

Over a four-week period beginning October 2, 40 case-patients and 83 eligible controls were reached by telephone and administered a questionnaire. Respondents were asked about the type of jobs performed during the tobacco growing season, work duration, self-reported use of protective clothing, exposure to wet tobacco leaves and working in wet clothing, and personal tobacco use.

Through observations of tobacco harvesting, NIOSH investigators identified body regions most likely to receive the highest exposures to nicotine through skin absorption. It was determined that the hands, forearms, thighs, and back were the areas which were most likely to become exposed through contact with moisture on the leaf surface.

The case-control study showed that ill workers were more likely than non-ill workers to have worn clothing soaked from wet tobacco. Ill workers were younger than non-ill workers. The incidence for developing GTS during the 1992 harvest season was approximately 10 per 1000 workers.

A case-control study prompted by 47 cases of green tobacco sickness in Kentucky identified wet clothing from exposure to moisture on leaves and young age as risk factors for disease. Recommendations designed to reduce exposure to wet tobacco and to increase awareness of the condition among farm workers, farm owners, and health care practitioners are included in this report.

KEY WORDS: SIC 0132 (Field Crops, Tobacco), Green Tobacco Sickness (Illness), Nicotine Poisoning, Tobacco Harvester

II. INTRODUCTION

On September 14, 1992, the National Institute for Occupational Safety and Health (NIOSH) received a report of 31 cases of green tobacco sickness (GTS) in tobacco harvesters who sought treatment in several south-central Kentucky hospital emergency departments. The report was made by an occupational nurse in Bowling Green, Kentucky who worked with the Occupational Health Nurses in Agricultural Communities (OHNAC)* Project of Kentucky. At the time of the initial call, there were 27 possible cases in the Bowling Green area, and an additional four likely cases in the Elizabethtown area. On September 15, NIOSH investigators traveled to the two areas in Kentucky to review the medical records of the ill workers. A medical records search was initiated in five hospitals. The State Epidemiologist for the state of Kentucky requested technical assistance from NIOSH on September 21 to investigate the reported cases of green tobacco sickness. On September 25, a NIOSH industrial hygiene team observed work practices of tobacco harvesting at two farms: one in Kentucky and one in Ohio. On September 28, investigators from NIOSH and occupational health nurses from the Kentucky OHNAC project initiated a case-control study in order to evaluate possible risk factors for the condition. Before the NIOSH investigation was initiated, OHNAC occupational health nurses had supplied emergency department physicians with literature about GTS, and one local newspaper published an article about it.

An interim report was submitted to the Kentucky Department for Health Services on December 17, 1993. Participants of laboratory testing were notified in October, 1992 of results of a test performed during illness; and again in March 1993 after a follow-up specimen was submitted for analysis.

III. BACKGROUND

A. General Description of Tobacco Harvesting

The tobacco harvesting season in 1992 began in late July and lasted approximately 8-9 weeks. Workers who pick tobacco begin work early in the morning. The tobacco leaves may be wet from dew or recent rainfall. The harvesters often become covered with a sticky gum from the leaves and drenched with moisture from the

* OHNAC is a national surveillance program conducted by CDC's National Institute for Occupational Safety and Health that has placed public health nurses in rural communities and hospitals in 10 states (California, Georgia, Iowa, Kentucky, Maine, Minnesota, New York, North Carolina, North Dakota, and Ohio) to conduct surveillance of agriculture-related illnesses and injuries that occur among farmers and their family members.

leaves while working. As the work day progresses, their skin is in continual contact with their wet clothing.

To begin the harvesting of tobacco, workers walk between the rows of tobacco laying down stakes which are used to collect the stalks. Workers then begin at the end of a row by placing a stake in the ground and putting a small conical spear on the end of the stick. The worker cuts the tobacco stalk at the base of the plant with a small hatchet in one sweeping motion while holding the top of the plant with the free hand. The cut stalk is then pushed through the spear and impaled on the stake; five stalks are placed on one stake. Once the stalks have been cut and left to dry for 1-2 days, the stakes are loaded onto a wagon and taken to a barn to be hung for drying (curing).

B. Workforce

The workforce engaged in tobacco harvesting is not a homogenous group. Harvesters may be tobacco farm owners, day laborers, migrant workers, or persons with full-time jobs who harvest on weekends. More men than women harvest tobacco. Persons as young as twelve or thirteen may be working in tobacco patches. There are many tobacco farms, ranging from a few acres in size to major operations. There is no organization that represents some or all workers. There are approximately 60,000 full and part-time tobacco harvesters in Kentucky, estimated from the average number person-hours per acre and number of acres planted with tobacco in Kentucky.¹

IV. EVALUATION METHODS

A. Industrial Hygiene

On September 25, 1992, NIOSH investigators visited two farms to observe work practices during the harvesting of wet, green tobacco. Regions of the body were identified where the potential for absorption was the highest, and observations were made of the type of clothing worn by the workers.

B. Medical

On September 15, 1993, a review of medical records for inpatient and emergency room patients was initiated at five OHNAC-participating hospitals in the Bowling Green and Elizabethtown areas, for a time period beginning in May, 1992. The record review identified 55 persons diagnosed with "green tobacco sickness", "nicotine poisoning", or other diagnoses compatible with GTS symptomatology (e.g., nausea). The record review was completed on October 2. On September 22, arrangements were made with the four of the five participating hospitals to collect urine

samples from any persons seen in the emergency departments and diagnosed with green tobacco sickness. The samples were analyzed by immunoassay at a NIOSH contract laboratory to measure levels of urinary cotinine (a metabolite of nicotine).

To evaluate possible risk factors associated with GTS, NIOSH investigators and occupational health nurses from the Kentucky OHNAC project conducted a case-control study. A case was defined as a person with an emergency department diagnosis of GTS or nicotine poisoning and whose recorded work history included tobacco harvesting at the time of illness. Forty-nine of the original 55 case-patients whose records were reviewed met the case definition, with episodes occurring between July 25 and September 19, 1992. Two cases were subsequently excluded from analysis because illness onset coincided with self-reported exposure to pesticides (which can induce similar symptoms). Non-matched controls were selected from tobacco workers without symptoms of GTS this year who were suggested by case-patients, local agricultural extension agents and community organizations. The use of varied sources for control ascertainment maximized the chance of selecting persons from the source population of tobacco harvesters. Over a four-week period beginning October 2, 40 of 47 case-patients (85%) and 83 of 101 (82%) eligible controls were reached by telephone and administered a questionnaire. Once contacted by the investigators, no one refused an interview. Respondents were asked about the type of jobs performed during the tobacco growing season, use of protective clothing, exposure to wet tobacco leaves, working in wet clothing, work duration, and personal tobacco use. Personal use of tobacco was categorized in three ways: a) reported use of any tobacco product b) reported use of cigarettes only c) reported use of smokeless tobacco products only. Protective clothing use was categorized as whether respondent reported having ever used gloves or plastic rain gear during the current harvesting season. Respondents were asked about the type of shirt and pants they usually wore while working in tobacco. The duration of time spent in the tobacco patch was measured as days/week; hours/day; and number of weeks during the current harvest season. Case-patients were asked additional questions about their episode of GTS.

Climatic data were obtained from the National Weather Service for weather stations near the residence of each ill worker. These data were examined to investigate the possible relationship between illness and rainfall. The climatic data were not used as an exposure variable to compare case-patients and controls, as controls were not time-matched to the date of illness onset for case-patients.

V. EVALUATION CRITERIA

Green tobacco sickness affects workers in contact with green tobacco^{2,4}. Nicotine poisoning is the most likely etiology, with the moisture on wet tobacco leaves the probable vehicle for dermal absorption of dissolved nicotine². This condition is characterized by nausea, vomiting, weakness, dizziness, and alterations in heart rate and blood pressure. It is self-limited and of short duration (1-2 days), but may be severe in nature². Use of protective clothing has been shown to reduce the amount of nicotine absorbed by workers in contact with green tobacco. For an intervention trial in North Carolina, a group of workers wore rubberized suits during morning hours. Those workers had minimal nicotine absorption, measured by urinary excretion of cotinine, compared with others who wore normal work clothing⁵. In a study from India, workers using rubber gloves had much lower urinary excretion of nicotine and cotinine, as well as fewer symptoms of GTS than controls⁶.

Symptoms of GTS are similar to those of organophosphate poisoning, which may lead to misdiagnosis by practitioners unfamiliar with GTS. In Kentucky, the final application of pesticides to tobacco plants occurs three to four weeks before harvest. The most commonly used agent is Orthene, an organophosphate pesticide that rapidly degrades, minimizing the risk of human health effects several days after application.

A test for urinary cotinines (a metabolite of nicotine) is used to measure absorbed or inhaled nicotine, and is often employed in epidemiologic studies of passive and active smokers.⁷ This test has also been employed in studies of nicotine absorption in tobacco workers^{5,6}, but concentrations that represent toxic levels have not been established.

VI. RESULTS AND DISCUSSION

A. Industrial Hygiene

Through observations of tobacco harvesting, NIOSH investigators determined that during harvesting, the hands, forearms, thighs, and back were the areas which were most likely to become saturated with moisture from tobacco leaves. Other work practices which may increase dermal exposure included the loading of tobacco onto wagons and the hanging of tobacco in barns; however, the degree of dermal exposure from these work practices appeared to be far less intense than that from actual harvesting. The tobacco harvesters reported that protective clothing is never worn, and that laundry bleach was often employed in removing black stains (residue from green tobacco) from their hands. Workers differed in experience level, and consequently, in their work practices. More experienced workers harvested tobacco more quickly and tended to have less contact with the plant.

B. Medical

Case-patient information:

The median age of the 47 identified case-patients was 29 (range: 14-54); 6 (13%) were female. One case-patient was hispanic, the other 46 were white. Twelve (26%) were hospitalized for periods of one to two days, and two of these (4%) required intensive care treatment for hypotension and bradycardia. All case-patients were initially treated in emergency departments with anti-emetic drugs, and 35 (74%) received intravenous fluids. Among the 40 (85%) who completed interviews, the median time from starting work in the morning to first feeling ill was 10 hours (range: 3-17 hours); most frequently reported symptoms included weakness (100%), nausea (98%), vomiting (91%), dizziness (91%), abdominal cramps (70%), headache (60%), and difficulty breathing (60%). The mean duration of illness was 2.4 days. Thirty-six (90%) had previous work experience with tobacco. Of these, 14 (39%) had sought medical care for symptoms suggestive of GTS in previous years. Seventeen (85%) of 20 cases ≥ 30 years of age attributed their illness to working in wet tobacco, compared to twelve (60%) of those under 30. No interviewed case-patient reported pesticide exposure within the 24 hours prior to becoming ill. It is thus unlikely that the affected workers were suffering from acute pesticide poisoning.

The crude two-month incidence rate of hospital-treated GTS among tobacco workers in the five-county study area was estimated to be 10/1000 workers. The denominator for this rate is based on an estimate of 78.8 person-hours worked per acre during tobacco harvest¹, the number of acres planted with tobacco, and an estimate of 256 harvest hours worked annually per worker (the median value reported by case-patients and controls combined). These figures generated an estimate of 4730 tobacco harvest workers in the five affected counties, of whom 47 sought medical treatment at local hospitals.

Representative hospital costs were calculated for three levels of care received by 31 case-patients treated at two participating hospitals. On average, fees were \$250 for out-patient treatment, \$566 for hospital admission, and \$2,041 for intensive care treatment. The medical costs for treatment are not inconsiderable, especially for day laborers who may have out-of-pockets costs for medical care as well as reduced income from loss of work time. Agricultural workers are specifically excluded from workers' compensation in the state of Kentucky, and some tobacco harvesters do not have any form of health insurance. In several instances, farm owners assumed the cost of medical care for uninsured employees.

Urine cotinine testing:

Very few new cases of GTS occurred after September 22, the date when hospitals were asked to collect specimens for urinary cotinine levels from all patients who presented with GTS. Specimens were collected from two case-patients at one of the participating hospitals. One of the case-patients smoked cigarettes and the other used chewing tobacco. The samples were analyzed by immunoassay at a NIOSH contract laboratory to measure levels of urinary cotinine. The same two persons resubmitted urines for cotinine levels approximately one month after they had been sick, during which time they had not worked in tobacco. The reported levels of urinary cotinine were very high for both tests (Table 1); therefore, the effect of occupational exposure to green tobacco could not be differentiated from heavy tobacco use. The test method and reference range were changed between the two tests, so the cotinine level during illness could not be compared the cotinine level during convalescence.

Rainfall:

Figure 1 shows the frequency of GTS cases by the amount of rainfall on the day preceding or the day of illness of case-patients. Three times as many cases occurred after days with 0.2 inches of rain or more compared with dry days, suggesting that wet working conditions are associated with green tobacco sickness. Rainfall data could not be considered an exposure variable for GTS in the case-control study because controls were not time-matched to case-patients for the day of illness onset.

Case-control study:

Table 2 describes the age and sex distribution of the case-patients and controls. Case-patients and controls had the same sex distribution but were substantially younger. Table 3 lists the results of stratified analyses which estimated the odds ratios and exact 95% confidence intervals for independent risk factors. The strongest risk factors associated from illness from this study were young age and becoming soaked from wet tobacco. Young age was found to be a strong risk factor regardless of how it was categorized. The estimated relative risk of a person under 30 developing GTS is 3.1. All 40 cases (100%) and 69/83 (83%) of the controls had worked in wet tobacco where their clothes became wet. Gender and work duration were not found to be associated with illness. Several potential work-related risk factors were associated with disease, but were not statistically significant. The odds ratio (OR) for reported use of any tobacco product (controlling for age) was 0.7, and the OR was 3.6 for not changing into dry clothes when wet, but the confidence intervals included one.

Older workers had less risk of developing GTS, possibly due to work practices which reduced contact with wet tobacco. This investigation revealed that older workers were more aware that working with wet tobacco could cause the illness. Another explanation for the age effect may be that workers prone to developing symptoms of GTS drop out of this work force at a young age (i.e., survival bias). Twenty of the interviewed case-patients indicated that they would not work in wet tobacco again, and three of those said they would avoid work in tobacco altogether. The finding that younger age increases GTS risk may be biased if the age distribution of selected controls does not reflect that of the source population of tobacco workers in the study area. Methods of control selection were employed to minimize this possibility.

Personal use of tobacco products may be weakly protective because of the development of tolerance to the effects of nicotine among regular tobacco users. This effect, however, was much less prominent than that reported previously in North Carolina (OR=0.06; CL=0.01,0.24).³ Tolerance may not be protective if the user's customary nicotine intake is substantially exceeded⁹, which may have occurred in this outbreak because of heavier than usual rains.

Other than wearing clothing which became wet with contact from wet tobacco, many of the specific behaviors or work practices involving direct dermal contact with wet tobacco leaves (eg: short sleeve shirts, no rain gear) were not statistically associated with GTS among the tobacco harvesters interviewed. This study was limited in its ability to detect important differences in the use of protective clothing and in the effect of wet climatic conditions because controls were not time-matched to cases. They could not therefore be queried about clothing worn or the weather on the specific work day that a case-patient became ill.

VII. CONCLUSIONS

Forty-seven cases of green tobacco illness were identified in two areas of South-Central Kentucky. The typical incidence of GTS during the tobacco-growing season is unknown in Kentucky. Improved case detection through increased surveillance of adverse health events in persons working in agriculture, as well as increased awareness of the condition through newspaper reports, may explain the large number of cases this harvest season. Uncharacteristically heavy rainfall during the 1992 harvest season may have increased incidence of the condition. Green tobacco sickness caused by working with wet tobacco may be preventable through the use of protective clothing which minimizes direct contact with wet tobacco leaves. The ill workers in this study

were more likely to have worn clothing soaked from wet tobacco than non-ill workers. Older workers were at lower risk, possibly because they had developed work practices which reduced exposure to wet tobacco.

VIII. RECOMMENDATIONS

The following recommendations are offered as prudent practices to prevent dermal exposure to wet, green tobacco and to disseminate information about the condition to tobacco harvesters, tobacco farm owners and health care practitioners.

1. In order to reduce the risk of developing GTS, exposure to wet tobacco should be avoided. Waterproof clothing is one means to minimize exposure. One study demonstrated that raincoats were effective in preventing absorption of nicotine while working in wet tobacco.⁵ Although waterproof clothing can minimize exposure, this benefit must be weighed against the potential risk of heat stress caused by wearing impermeable clothing in hot weather. Therefore, further research is needed before recommendations can be made on specific types of waterproof clothing that may be worn during tobacco harvesting without causing heat stress. Wearing gloves which cover both the hands and the forearms will further reduce contact when handling green tobacco, and should be replaced as the glove surface integrity deteriorates. Water-proof rubber gloves which will allow the worker to maintain manual dexterity should provide adequate protection. Polyethylene and ethylene vinyl alcohol gloves have both been shown to provide adequate protection against the absorption of nicotine in non-agricultural settings if exposures do not exceed a 4-hour time period.⁹ Leather or cotton (canvas) gloves, as well as leather boots, are not adequate for protection since they absorb water.
2. If any worker's clothes become saturated with moisture on the green tobacco leaf, the worker should change into dry clothes as soon as possible. Therefore, workers should be advised to bring a change of clothes to work every day.
3. Surveillance in local hospitals and clinics during tobacco growing seasons should continue in order to determine if green tobacco sickness is a regular occurrence or whether this outbreak was due to an unusually wet growing season. In the long run, surveillance may aid in evaluating the implementation and efficacy of preventive measures.
4. Educational activities should be designed to reach farm workers, farm owners, and health care practitioners. Owners of tobacco farms should inform their employees of the hazards associated with harvesting wet tobacco and the importance of minimizing contact with tobacco. The routes of exposure and the symptoms associated with the disease should also be discussed with each worker. Information on the disease (signs and symptoms, causes and preventive measures) should be provided to health care professionals and institutions that are located in tobacco-growing regions of Kentucky. A careful work history will help to rule out conditions which may be confused with GTS, such as organophosphate poisoning, heat exhaustion, or gastroenteritis.

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Copies of this report have been sent to:

1. Kentucky Department for Health Services, Frankfort, Kentucky
2. Two tobacco farmers in Ohio and Kentucky who made their farms available for work practice observations.
3. Tobacco harvester-participants of the case-control study.

Tobacco harvesters are seasonal workers and may no longer be working at the same location when this report is distributed. Therefore, the posting regulations for the purpose of informing affected employees by posing this report in a prominent place accessible to the employees for a period of 30 calendar days are not applicable.

Table 1

Results of Urinary Cotinine Levels from Two Persons at
Time of Illness and One Month Later

	September 21	October 21
<u>patient A</u>		
a. level (range for non-smoker)*	7.3 µg/ml (0.0-0.5)	2.52 µg/ml (0.0-0.19)
b. circumstances	symptomatic, working in tobacco	not ill, no work in tobacco previous month
c. tobacco use	chewing tobacco	
<u>patient B</u>		
a. level (range for non-smoker)	11.3 µg/ml (0.0-0.5)	3.50 µg/ml (0.0-0.19)
b. circumstances	symptomatic, working in tobacco	not ill, no work in tobacco previous month
c. tobacco use	cigarettes	

* The test method and reference range were changed in the interim period between tests, so results could not be compared. The reference ranges for smokers were reported by the laboratory as follows: For the test performed Sept. 21: light smokers = 0.6-1.0; moderate smokers = 1.1-2.0; heavy smokers = > 2.0. For the subsequent analysis, the reference range for all smokers was reported as 0.2 or higher.

Table 2

Characteristics of Cases and Controls
Green Tobacco Sickness

	Cases	Controls
Age:		
median	29	39
range	(14-54)	(16-70)
Sex:		
female	6 (13%)	11 (13%)
male	41 (87%)	72 (87%)
total	47	83

Table 3
Risk Factors for Green Tobacco Sickness from Case-Control Study

<u>EXPOSURE</u>	<u>ODDS RATIO*</u>	<u>EXACT 95% CI</u>	<u>EXACT P VALUE</u>
age			
<30 v. >=30	3.1	(1.4 - 7.0)	.004
<40 v. >=40	4.6	(1.9 - 11.9)	<.001
GTS diagnosis previous year	3.3	(0.61 - 20.32)	ns**
wet clothes from wet tobacco	infinite	(1.8 - infinite)	.003
not changing out of wet clothes	3.6	(0.5 - 85.1)	ns
current use of any tobacco products	0.7	(0.32 - 1.5)	ns
harvesting > 4 days/week	1.0	(0.49 - 2.3)	ns
harvesting > 7 hours/day	0.96	(0.42 - 2.2)	ns
female v. male	0.94	(0.27 - 2.8)	ns
non-use of gloves	0.78	(0.32 - 1.9)	ns
sleeveless or no shirt	1.1	(0.34 - 3.4)	ns
short pants	1.8	(0.41 - 7.7)	ns
no rain gear	2.5	(0.26 - 121.2)	ns

* from a Maximum likelihood estimate of the odds ratio

** p value > .10 (non-significant) Exposure variable