HETA 87-042-1869
FEBRUARY 1988
FLORIDA DEPARTMENT OF HEALTH
AND REHABILITATIVE SERVICES
JACKSONVILLE, FLORIDA

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I. SUMMARY

On October 21, 1986, the National Institute for Occupational Safety and Health (NIOSH) received a request from the State of Florida Department of Health and Rehabilitative Services (DHRS), to evaluate dermatologic conditions (red rashes, dryness and chapping) in public health laboratory workers processing Neisseria gonorrhoeae (GC) culture plates.

To determine if the reported skin conditions in workers were related to occupational exposures, NIOSH investigators visited five of the seven state public health laboratories on January 12-23, 1987. A questionnaire was administered to all laboratory personnel present on the dates of visits to the individual laboratories. Ninety-nine (97%) of the 102 total laboratory personnel employed completed the self-administered questionnaire. Cases were defined as individuals with a red rash or excessive dryness and chapping on the hands or arms, lasting one or more days, and occurring within the past year.

A total of 54 workers reported exposure to the oxidase reagents, used in the preliminary identification of Neisseria gonorrhoeae cultures. Twenty-four (44%) of those workers exposed to the oxidase reagents were identified as cases (Relative Risk (RR) = 2.0, Confidence Interval [CI] = l.l-3.6). The twenty-four oxidase-exposed cases were skin patch tested with the oxidase reagents; seven (29%) individuals had positive tests for allergic contact dermatitis. This represents a sensitization rate of at least 13% among all 54 workers exposed to the oxidase reagents. An association was also found between non-sensitized cases of dermatitis and the degree of exposure to the oxidase reagents.
Workers with the greatest degree of exposure were at increased risk of becoming non-sensitized cases.

Based upon the results of this investigation, the investigators concluded that there was a health hazard from exposure to oxidase compounds at public health laboratories of the Florida Department of Health and Rehabilitative Services. Recommendations for reducing exposure to oxidase reagents and reassigning sensitized workers are contained in Section VIII of this report.

KEYWORDS: SIC 8071; P-phenylenediamine (CAS:l06-50-3); p-diaminobenzene (CAS:l06-50-3); 1,4 diaminobenzene (CAS:l06-50-3); ursol; oxidase; p-aminodimethylaniline oxalate (CAS:2463l-29-6); N,N-dimethyl-p-phenylenediamine (CAS:l05-l0-2); N,N- dimethyl-p-phenylenediamine monohydrochloride (CAS:2052-46-2) ; N,N- dimethyl-p-phenylenediamine dihydrochloride (CAS:536-46-9); N,N,N',N'-tetramethyl-p-phenylenediamine dihydrochloride (CAS:637-0l-4); allergic contact dermatitis; skin rash.

II. INTRODUCTION

In October 1986, NIOSH received a request for a health hazard evaluation from the Office of Laboratory Services at the Florida Department of Health and Rehabilitative Services. The request was initiated as a result of several reported cases of severe dermatitis in laboratory workers at five of the seven Florida State public health laboratories. Workers involved with Neisseria gonorrhoeae (GC) culture plate processing, and in particular having contact with oxidase reagents (used in the preliminary identification of Neisseria gonorrhoeae species) or residue from carbon dioxide generating tablets, were reported to have the most severe skin problems. NIOSH investigators conducted field evaluations of this problem during January 12-23, 1987.

The preliminary findings of this investigation were presented by telephone on March l5 to the Office of Laboratory Services, and a written presentation of the initial results of the study was sent at that time. The preliminary results were presented to administrative staff and employees at the Florida DHRS, Miami laboratory on May l8, l987.

III. BACKGROUND

The Florida Department of Health and Rehabilitative Services is centered in Jacksonville, Florida, where administrative offices, as well as a public health laboratory are located. In addition, there are six regional laboratories located in Miami, Orlando, Pensacola, Tallahassee, Tampa, and West Palm Beach. At these public health facilities, the general public is offered testing for a number of communicable diseases. One of the busiest operations the laboratories are involved in is testing and screening for sexually transmitted diseases. The processing of Neisseria gonorrhoeae cultures comprises a large portion of that work.

Screening and testing for GC begins with the collection of a urethral, vaginal, anal or pharyngeal swab, which is plated onto culture media at the time of collection, usually in area hospitals, clinics or emergency rooms. Plated specimens are then placed in individual plastic bags with a carbon dioxide (CO_2) generating tablet, which reacts to create an anaerobic environment to support growth of GC during transport. Laboratory slips, which identify the patient, specimen source and type of test to be completed, are either placed inside the plastic bags with the culture plates or are attached to the outside of the bags. The bags are then transported to public health laboratories for processing.

Once received at the laboratories, approximately 24-48 hours later, the bags are opened and laboratory slips are removed. Technicians apply a few drops of 1% oxidase reagent from a plastic squirt bottle onto thoseculture plates with positive growth (usually about 10%-15% of all plates received). Neisseria species turn a dark purple or black color within a few minutes. Untreated colonies are gram-stained and/or sub-cultured. Technicians then treat the entire surfaces of all plates without growth (about 85%-90% of all plates received) with a larger volume of oxidase reagent to detect micro-colonies that might not be visible to the unaided eye, a technique referred to as "plate flooding." All plates are then discarded.

Initial telephone interviews conducted by NIOSH with all seven laboratory directors revealed that five of the laboratories had one or more employees with dermatitis. The five laboratories employ a total of 102 workers, and are located in the cities of Jacksonville, Miami, Orlando, Tallahassee, and Tampa. The investigation focused primarily upon employees at these five laboratories.

IV. EVALUATION DESIGN AND METHODS

Employees at the five public health laboratories were evaluated by use of a self-administered questionnaire (see Appendix). The questionnaire was designed to evaluate and characterize laboratory personnel by age, race, sex, occupational history and exposures, personal and family history of allergy, and the occurrence of skin conditions within the past year.

Individuals were designated as cases of dermatitis if they reported a rash (red, inflammed skin) or dryness and chapping of skin, occurring on the upper extremities, within the past year. Cases who worked in the processing of GC culture plates, (which includes plating, incubating, gram staining, transporting, applying oxidase reagent, handling GC laboratory slips, etc.) were given closed skin patch tests to evaluate sensitivities to work related exposures.

The skin patches contained test substances consisting of three different oxidase reagents at concentrations of 1% by weight in petrolatum; they included:

1) p-aminodimethylaniline oxalate, Miami laboratory;
2) p-aminodimethylaniline oxalate, Jacksonville laboratory;
3) N,N,N',N'-tetramethyl-p-phenylenediamine dihydrochloride, Orlando laboratory;
4) and N,N-dimethyl-p-phenylenediamine monohydrochloride, obtained from the Cincinnati Health Department laboratory (compounds 1 and 2 above are identical).

Also included in the patch testing were paraphenylenediamine at a concentration of 1% by weight in petrolatum, the carbonate (CO_2- generating) tablet at a concentration of 10% by weight in petrolatum, and a blank of petrolatum. Paraphenylenediamine and the fourstructurally related oxidase compounds were tested at concentrations as recommended for paraphenylenediamine by the North American Contact Dermatitis Group (NACDG) and the International Contact Dermatitis Research Group (ICDRG).[1]

Where indicated by their use in the individual laboratories, liquid hand soaps and laboratory countertop disinfectants were incorporated into the patch test at a strength of 5% dilution in distilled water, or at actual working concentrations if these were less than 5% of full strength. Stronger concentrations of soaps or disinfectants were also tested by the uncovered patch test method.[2]

Standard Finn chambers on Scanpor were used to apply the closed patch test.[3,4] Patch tests were applied to the lateral aspect of the upper arm, removed at 48 hours, and interpreted at 72 hours after initial placement. The test was interpreted at 72 hours as: negative (-), indicating "no reaction"; doubtful reaction (?+); weak (1+), indicating a non-vesicular reaction; strong (2+), indicating an edematous or vesicular reaction; extreme (3+), indicating a bullous or ulcerative reaction; and IR, indicating an irritant reaction, rather than an allergic skin reaction. The above grading scale recommended by Wilkinson et. al.,[5] is the most widely used interpretation scheme among dermatologists today.

A standard Chi-square test was then used to compare cases to noncases with respect to race, sex, history of atopy, history of eczema, family history of allergy, degree of handwashing, use of laboratory countertop disinfectants, and exposure to oxidase reagent and/or the CO_2-generating tablet. A Fisher's Exact Test was used to compute p-values when expected cell sizes were less than 5 in the 2 X 2 contingency tables.[6] Further analyses examined subgroups of the cases (i.e. sensitized cases and non-sensitized cases) compared to noncases.

Next, a series of 2 X 2 contingency tables were constructed to look at a possible effect modification between exposure to oxidase and other risk factors for dermatitis Only non-sensitized cases and noncases were used in the analysis. Sensitized individuals were excluded in the comparisons.

The final analyses involved the use of Mantel's Chi-square test for trend[(7)] to incorporate duration and intensity of exposure into the analyses. Exposure variables were developed using the worker's length of employment in the laboratories, the number of years of their exposure to the oxidase reagents and CO_2-generating tablets, and the average number of culture plates they applied oxidase reagent to(and/or plates handled and contained in plastic bags with the CO_2-generating tablet) in an average week. For example, the exposure variable OXDOSE was calculated as the product of the average number of plates oxidaswas applied to in a typical workweek multiplied by the total number of weeks worked at this job.

The exposure variable (OXDOSE) had a very high variance; therefore, Log_0 values of OXDOSE were used in the test for trend analyses. Five levels of exposure were used over the range of Log_0 OXDOSE values, and this was

done by two methods. Cases were compared to noncases using levels of exposure determined by equal increments of exposure over the dosage range, and then by an equal distribution of study subjects over the dosage intervals. These comparisons were repeated for non-sensitized cases and sensitized cases. In the test for trend using only sensitized cases and exposed noncases, two exposure categories were used. This was because the small number of sensitized cases did not allow at least one member of that group to be present in each dosage interval when greater than two intervals were used, and there were no sensitized cases in the zero exposure category.

V. EVALUATION CRITERIA

Di- and tetra-methyl-substituted paraphenylenediamine compounds and their mono- and dihydrochloride salts are currently used as oxidase reagents at public health, private and hospital based sexually transmitted disease laboratories and microbiology departments for the preliminary identification of Neisseria gonorrhoeae species in culture growths. These compounds are very similar to p-phenylenediamine (PPD) (FIGURE 1), which is used in permanent hair dyes, fur dyes, leather processing, rubber vulcanization, printing inks, photographic developing, x-ray fluids, lithography, and in the manufacture of azo dyes.

1. Human Health Effects

Although there are no published reports of health hazards associated with di- and tetra-methyl-substituted paraphenylenediamine compounds (oxidase reagents), PPD and its derivatives are known to cause adverse health effects in other groups of workers and consumers. Several reports have linked the use of PPD in the fur-dyeing industry with cases of occupational contact dermatitis and asthma.[8] Contact dermatitis has also been reported secondary to wearing furs dyed by PPD compounds[9]. Paraphenylenediamine and closely related chemical derivatives (especially isopropyl-aminodiphenylamine or IPPD) are used as accelerants in the vulcanization of rubber and as antioxidants in the final product. Rubber workers have been identified as a high risk group for contact dermatitis as a result of their close work with chemicals in general, and more specifically due to work with PPD related derivatives.[10,11] IPPD sensitivity has even been reported to develop in one purchaser of a new automobile, who, after several washings of the vehicle, developed allergic contact dermatitis to IPPD contained as an antioxidant in the car's tires and bumper guards.[12]

The use of paraphenylenediamine as an antioxidant in the black rubber of eyelash curlers has resulted in contact dermatitis of the eyelids.[13,14] PPD derivatives are used in the manufacture of azo and aniline dyes and inks. PPD has also been implicated as a cause of occupational dermatitis in a worker exposed to stamp pad ink.[15]

The largest and most extensively studied group of workers exposed to PPD are hairdressers. These workers are commonly exposed to PPD contained in permanent hairdyes. Sensitization to PPD was reported to be 31% among hairdressers with hand eczema in one study,[16] and as many as 45% of hairdresser patients in a more recent study were reported to have positive patch tests to PPD.[17]

In addition to being a skin irritant, PPD is a potent skin sensitizer. Tests conducted in a normal, previously unexposed population produced sensitization in 53% of those individuals[18] (the standardized method of predictive testing used a modified Draize procedure[19] and employed 200 human subjects who were patch tested with 1.0% concentrations of PPD). Human maximazation tests conducted by Kligman showed a 100% sensitization rate in 24 subjects.[20] Another study suggests that PPD compounds alone are responsible for as much as 8% of all cases of occupational dermatitis in Sweden.[21]

Further evidence of the strong sensitizing ability of PPD may be supported by the FDA complaint file in 1974, where as many as 1.9% (639) of all consumer complaints were registered against oxidative hair

dyes that contain PPD or its close chemical derivatives.[22] Hair-dye users are, in fact, cautioned to patch-test themselves behind the ear prior to each use of the dye.

The use of PPD and its close chemical derivatives is widespread throughout industry, and cross-sensitization to the derivatives is known to occur. In addition, cross-reactions may occur in individuals secondary to cross-sensitization between PPD (as well as close chemical derivatives of PPD) and a number of other compounds and medications. For instance, PPD-sensitized individuals have had reported cross-reactions with azo and anthraquinone dyes, local anesthetics (procaine and benzocaine), sulfonamides, para-aminosalicylic acid, hydrochlorothiazide, carbutamide, pyrogallol and para-aminobenzoic acid (PABA)-based sunscreens.[23] Individuals sensitive to PPD and its closely related chemical derivatives are at risk for cross-reaction with other compounds and medications, even though the risk for this is usually low.

A number of epidemiologic studies have attempted to determine whether there is an association between the use of hair dyes and cancer.[24-28] The findings have been equivocal and conflicting. One NIOSH study involving the analysis of 4l7,795 Social Security disability awards made to female workers between l969 and l972 showed elevated proportional morbidity ratios among cosmetologists and hairdressers for cancer of the digestive organs, respiratory system, trachea, bronchus and lung, breast and genital organs.[29] Although such findings are consistent with the hypothesis that cosmetologists and hairdressers may be at risk of developing a neoplasm due to occupational exposures (e.g. to PPD and its chemical derivatives), these workers come into contact with a large variety of substances, only one of which is PPD. As such, it is not possible to attribute any excess incidence of cancer to hair dyes in general, or to any singular chemical contained in their formulations.

2. Toxicity Data and Laboratory Studies

Oxidase reagents currently in use in laboratories for the identification of N. gonorrhoeae species are the following: l) N,N-dimethyl-paraphenylenediamine and its mono- and dihydrochloride salts; 2) N,N-dimethyl-paraphenylenediamine oxalate (p-aminodimethylaniline oxalate); and 3) N,N,N'N'-tetramethyl-paraphenylenediamine dihydrochloride. Of the aforementioned compounds, very little or no data was found in the literature with respect to human or animal toxicity except for the compound N,N-dimethyl-paraphenylenediamine. The lowest published toxic dose for human skin of this latter compound was reported to be l4 mg/kg.[30] The lowest lethal dose by oral ingestion (LDLo) in the rat for this compound was 50 mg/kg.[3l] The LDLo in rats for N,N-dimethyl-paraphenylenediamine monohydrochloride was l00 mg/kg.[32]

Although no toxicity data exists for N,N- dimethyl-paraphenylenediamine, N,N,N',N'-tetramethyl-paraphenylenediamine dihydrochloride or para-aminodimethylaniline oxalate, some data does exist for very similar compounds. Paraphenylenediamine monohydrochloride has a reported LDLo of l00 mg/kg when administered orally to rats.[33] PPD dihydrochloride was lethal to 50 percent (LD_{50}) of rats when administered at a dose of l47 mg/kg.[34]

A review of studies conceming the carcinogenic risk of this chemical by the International Agency for Research on Cancer (IARC) in l978 deemed the data on PPD to be insufficient to make an evaluation regarding its carcinogenicity.[35] A study completed the following year on the bioassay of this compound for possible carcinogenicity concluded "there was no convincing evidence that dietary administration of p-phenylenediamine dihydrochloride was carcinogenic in Fischer 344 rats or B6C3Fl mice."[36]

Tetramethyl-paraphenylenediamine has also undergone rudimentry testing for toxicity in rats. An oral LDLo for this chemical was reported at 500 mg/kg.[37]

The most extensive data on the toxicity of these compounds is found concerning paraphenylenediamine (PPD) itself. Mild skin irritation was shown when PPD was tested on skin at concentrations of 250 mg/24H in human subjects as well as dogs, rabbits, pigs and guinea pigs.[38] The oral LD_{50} for rats exposed to PPD has been reported at 80 mg/kg and the LDLo was found to be at l00 mg/kg for cats and 250 mg/kg in rabbits.[39-41] Hanzlik has reported an LDLo of l70 mg/kg in rats and 200 mg/kg by oral ingestion in cats.[42] A TLV for PPD has been recommended at 0.l mg/m^3 for skin as suggested by Goldblaat with regard to industrial exposure in Britain.[43,44]

VI. RESULTS

Of the 102 workers employed at the five laboratories surveyed, 99 (97%) completed the self-administered questionnaire. The majority of respondents (68%) were female, almost half (46%) were white, and they ranged in age from 20 to 68 years, with a mean age of 42.6 years (TABLE 1).

Thirty-four (34%) laboratory personnel reported a skin condition that met the case definition. When compared to noncases, cases did not differ significantly with respect to age, race or sex (TABLE 2). Furthermore, no association was seen between being a case and having a personal history of atopy, eczema or family history of allergy, the degree of handwashing or use of laboratory countertop disinfectants.

The percentage of cases among laboratory workers using oxidase reagent was twice that of other workers, and this difference was unlikely to have been explained by chance (RR = 2.00, X^2= 5.38, [CI] l.ll,3.60) (TABLE 2). This association was also noted for CO_2-generating tablet exposure (RR = 2.25, X^2= 7.67, [C.I.] l.30,4.82. Exposures to oxidase reagent and the CO_2-generating tablet were very similar, and the following should be noted. Ten of the thirty-four cases of dermatitis had no exposure to the oxidase reagent and 8 had no exposure to the CO_2-generating tablet. All cases exposed to oxidase (24) had simultaneous exposures to the CO_2-generating tablets and only 2 of the 26 cases exposed to the CO_2-generating tablet had exposure to that alone. Among the 65 noncases, thirty reported exposure to oxidase and 33 had exposure to the CO_2-generating tablet. Again, all noncases exposed to oxidase reagent had simultaneous exposure to the CO_2-generating tablet and only 3 noncases of the 33 exposed to the CO_2-generating tablet had exposure to that substance alone. Thus, the close covariance of oxidase and CO_2-generating tablet exposure did not permit assessment of a risk for dermatitis to either compound alone.

Workers were skin patch tested if they satisfied the case definition for dermatitis and were exposed to some aspect of GC culture plate processing. Four cases were not patch tested since they did not meet the exposure criteria. Three other cases declined the skin patch test (two of whom had exposure to GC plate processing but not to oxidase reagent). Thus 27 of the 34 cases underwent patch testing.

Seven (26%) of the 27 cases tested had positive reactions, all strong, to all 4 oxidase reagents (TABLE 3) and were considered sensitized to the oxidase reagents. The lowest possible sensitization rate among the 54 oxidase exposed workers was thus l3%, assuming all sensitized individuals were among those patch tested. Of the 24 cases reporting exposure to oxidase reagents, the sensitization rate was 29%. These individuals not only reacted to the specific oxidase reagent used in their respective laboratory, but also showed cross-sensitization to the other two chemically related reagents, which they had never worked with. Two of the seven oxidase-sensitized individuals exhibited a weak cross-sensitization to paraphenylenediamine. One of the seven individuals also showed sensitization to "Septisol," a laboratory countertop disinfectant solution. None of the individuals tested showed evidence of allergic skin reactions to CO_2-generating tablets, or to liquid hand soaps.

For purposes of further analysis, cases of dermatitis were sub-classified into sensitized (positive patch test) and non-sensitized cases to oxidase reagent. The group of non-sensitized cases is comprised of those workers with red rashes or dry chapped skin that were not found to have sensitivity to oxidase reagent on skin patch testing. Also included in this group are 3 cases who refused patch testing (none of whom had red, inflamed skin, and 2 who had no oxidase exposure), and four cases who had no exposure to any aspect of GC plate processing.

Only the exposures to the oxidase reagent and CO_2-generating tablets were found to increase a subject's risk of sensitization (TABLES 4a & 4b). There were no statistically significant associations between any of the potential risk factors and non-sensitized case status.

The next analysis examined the effect certain risk factors had on the risk of developing non-allergic (non-sensitized) dermatitis while controlling for oxidase exposure (TABLE 5). Workers exposed to oxidase reagent and certain other risk factors were not found to be at greater risk than workers exposed to oxidase reagent alone. However, for workers exposed to oxidase reagent, excessive handwashing was protective against non-allergic dermatitis.

On the average, sensitized workers applied oxidase to three times as many culture plates as the oxidase exposed noncases (TABLE 6). Little difference was seen between non-sensitized cases and noncases with respect to oxidase exposure. The mean total culture plates to which oxidase was applied by a worker during their career (OXDOSE) for non-sensitized cases and oxidase exposed noncases was 256,990 and 253,6l3, respectively. With regard to the CO_2 tablet exposure, exposed noncases handled l.4 times as many culture plates in plastic bags containing the CO_2-generating tablet as did sensitized cases. Little difference was seen between non-sensitized cases and exposed noncases with regard to this exposure (the mean CO_2 dose for non-sensitized cases and CO_2 tablet exposed noncases was 2l8,667 and 2l7,3l5 total culture plates handled respectively).

A general test for trend[45] was computed employing the Log_{10} values of cumulative oxidase reagent exposure (OXDOSE). The relative risk for contact dermatitis (as defined by questionnaire) increased with increasing exposure to oxidase reagents (TABLES 7 and 8). A slight drop in the risk of dermatitis was noted in the group with greatest exposure, compared to the preceding group. The X^2 tests for trend using equal dosage intervals and equal distribution of cases and noncases were both highly significant (X^2= 7.94, $p<.005$ and X^2= 8.24, $p<.005$, respectively).

Using the same method, the non-sensitized cases were compared to noncases with respect to cumulative exposure to oxidase (TABLES 9 & l0). Workers in the highest exposure category were 2.4 times as likely to have irritant contact dermatitis when compared to the unexposed workers. By each method of calculation, the X^2 test for trend remained significant (X^2= 3.94, $p<.05$ and X^2= 4.13, $p<.05$,), indicating an upward trend of risk for dermatitis with increasing levels of exposure.

Finally, the sensitized cases and exposed noncases in the highest exposure group were compared with those in the lower exposure group. Risk of sensitization was primarily limited to the most highly exposedgroup (TABLES 11 & 12). Depending on how exposure groups are separated, the workers with greatest oxidase exposure were 4.2 to 6.0 times as likely to be sensitized as workers in the lower exposure category.

VII. DISCUSSION AND CONCLUSIONS

Laboratory workers were evaluated at five Florida State public health laboratories where there were reports of occupationally related skin conditions. Two state laboratories (West Palm Beach and Pensacola laboratories) did not report cases of dermatitis and were not investigated. The West Palm Beach and Pensacola laboratories handled far fewer GC specimens than the other 5 laboratories, neither used the oxidase plate-flooding method, and one applied oxidase reagent to the culture plates with an enclosed, glass pipetting system, rather than plastic squirt bottles. Thus, worker exposure to the oxidase reagents was probably much less than in the 5 laboratories investigated.

This investigation details the occurrence of Type IV cell-mediated (delayed hypersensitivity) skin reactions in state public health laboratory workers exposed to oxidase reagents. In addition, cases of irritant contact dermatitis were also associated with exposure to these reagents. These findings, and other comparisons between cases and noncases, may be challenged for two reasons: l) workers not exposed to chemicals in the processing of GC culture plates were not patch tested, and 2) exposed asymptomatic workers (exposed noncases) were not patch tested. These individuals were not tested because of the risk of sensitizing them from substances contained in the patch test itself.

From the standpoint of immunologic theory, an individual's immune system must be presented with an antigenic material before it can develop future, Type IV, delayed hypersensitivity responses, as occurs in allergic contact dermatitis.[46] Unexposed workers should not have been sensitized, then, as a result of workplace exposure. Furthermore, exposure to these oxidase compounds outside of work was highly unlikely.

Exposed noncases were not patch tested and were also assumed to be non-sensitized. A worker would need at least two incidents of direct skin contact with oxidase reagent before becoming symptomatic, thus it was improbable that a worker would have experienced sensitization but no symptoms. Also unlikely is the possibility that a sensitized worker would not have recognized the severity of symptoms which present with allergic contact dermatitis, leading to the eventual misclassification and non-testing of that worker.

Workers not tested may have been cross-sensitized to oxidase reagents by similar compounds in their environment, such as p-phenylenediamine contained in hair dye products. However, only two of the seven oxidase-sensitized individuals in this study exhibited weak positivepatch test results to p-phenylenediamine. These two workers had weaker reactions to p-phenylenediamine than to the oxidase reagents tested. Had their initial sensitization occurred as a result of p-phenylenediamine exposure (i.e. in hair dyes) they would be expected to exhibit at least as strong a reaction to p-phenylenediamine as to oxidase reagents. No other workers tested showed sensitization to p-phenylenediamine, and no study participants reported on the questionnaire skin conditions resulting from hair dye use. Thus cross-sensitization does not appear to be a means by which any laboratory worker would have been sensitized to the oxidase reagents.

With the above considerations in mind, a major assumption in these analyses was that all oxidase sensitized workers were included in the group of workers patch tested.

The NIOSH medical investigators found 7 cases of allergic contact dermititis among technicians who process gonorrhea culture plates and apply oxidase reagents. This represents a minimum sensitization rate of l3% among the exposed workers. These workers also demonstrated l00% cross-sensitization to similar oxidase reagents used in other laboratories. Observations of work practices and interviews with employees by NIOSH investigators revealed that maximum opportunity for accidental skin contact occured when negative plates were flooded with the oxidase reagents, and subsequently discarded.

Work practices varied considerably throughout the 5 laboratories visited, as did the volume of gonorrhea culture plates handled on a daily basis. Work areas were noted in some laboratories where considerable splashing of oxidase reagent had occurred on the countertops, walls and floors. Technicians confirmed this was most apt to occur during discard of the plates after flooding them with oxidase reagent. Four of the 5 laboratories which flooded negative growth plates with oxidase reagent, used plastic squirt bottles to accomplish this. Oxidase reagents were noted to leak out around the necks of these bottles as evidenced by the blackened outside surfaces. The one laboratory (Orlando), which uses disposable glass Pasteur pipettes to apply oxidase to the gonorrhea culture plates, had no workers with allergic or irritant contact dermatitis to oxidase reagents.

Workers varied in their use of protective disposable gloves when applying the oxidase reagent to gonorrhea culture plates. When gloves were worn by technicians, they were the disposable latex type, which are in fact permeable to the oxidase compound. Thus, reagent penetrating the gloves may be trapped against the skin, increasing the risk of dermatitis.

Workers also come into contact with powder from the CO_2-generating tablets, which had been improperly crushed and placed into the plastic bags when the cultures were originally plated. We found that this exposure also resulted in an increased risk of developing dermatitis. This may be a spurious association considering that exposure to the CO_2 tablet/powder parallels exposure to the oxidase reagent. However, excessive exposure to the tablets and powder, which contain sodium bicarbonate and citric acid, could be expected to cause drying and chapping of skin, and other imitant symptoms. Damaged skin may be a less effective barrier to chemicals, and this may increase the risk of sensitization of individuals also exposed to oxidase reagent.[47]

Finally, there is a dose-related association between exposure to oxidase reagent and dermatitis. This relationship is most likely due to the increased probability of skin exposure as workers apply oxidase to and dispose of increasing numbers of culture plates, thus emphasizing the fact that every precaution should be employed to limit worker exposure to this compound to an absolute minimum.

VIII. RECOMMENDATIONS

NIOSH investigators found a high rate of allergic contact dermatitis in laboratory workers exposed to oxidase reagents. Therefore, laboratory employees who work with oxidase reagents and are reporting redness and inflammation of the skin should be patch tested for contact allergy to the oxidase reagents. The test should include a mixture of the reagent in petrolatum at a concentration of 1% by weight. It should also be noted that paraphenylenediamine is not an acceptable patch test substitute for the actual oxidase reagents used in laboratories, due to the low rate of cross-sensitization and poor reactivity demonstrated in this study.

Laboratory workers who are found to have allergic contact dermatitis to oxidase reagent after skin patch testing should be transferred to other areas of the laboratory where they will not have contact with these oxidase reagents. Gloves will not afford adequate protection once sensitization has occurred.

Laboratory technicians who have not been sensitized should use disposable vinyl gloves when working with the oxidase reagents, since these will give greater protection from contact with the reagent, than the more permeable latex gloves. After every instance of work with oxidase reagent, employees should remove the protective gloves and wash their hands with a mild detergent soap and copious amounts of water.

Work practices should also be modified to minimize the accidental spillage that occurs in the application of oxidase reagent and in the disposal of the culture plates. This includes the use of disposable glass or plastic pipettes, rather than plastic squirt bottles, to apply oxidase reagent. In addition, to avoid accidental spillage of reagent onto them, laboratory slips that accompany the culture plates should be kept separate when oxidase is applied. Also, when plates are discarded, care should be taken to avoid excessive splashing and drippage of the reagent. Workers who sterilize the discarded plates should be made aware of the disposal bag's contents.

To avoid inadvertant exposure of other workers to accidentally spilled reagent, laboratory countertops where culture plates are placed for the purpose of oxidase application should be cleaned thoroughly after this process is completed.

Finally, the practice of "flooding" negative growth Neisseria gonorrhoeae plates should be reevaluated, since this generates a large volume of reagent which can be easily spilled when plates are discarded. The Center for Infectious Diseases at the Centers for Disease Control, which is responsible for recommending laboratory procedures and methods, has been made aware of the cases of sensitization to oxidase reagent. The process of "plate flooding" will be reviewed in light of this risk of sensitization to laboratory workers.

With respect to the secondary problem of possible irritant contact dermatitis related to exposure to powder from the CO_2-generating tablet, technicians should be advised to wear protective disposable gloves when removing culture plates from plastic bags in which the tablets are shipped with the plates. Laboratory directors should advise hospitals, clinics and emergency rooms of the proper method of placing the tablets into the plastic bags at the time the culture is obtained. This would include tearing open the foil envelope to expose the tablet contained inside, but the tablet need not be removed from the foil envelope. Furthermore, it should be stressed that the CO_2-generating tablet should not be crushed to powder form and dumped into the bag. Preferably, laboratory slips which accompany the culture plates should be attached to the outside of the plastic bags to avoid their unnecessary contamination with residue from the CO_2-generating tablet or the contents of the culture plates.

IX. REFERENCES

1. Fregert, S. Manual of Contact Dermatitis. Chicago: Year Book Medical Publishers, Inc., 1981.

2. Cronin, E. Contact Dermatitis. New York: Churchhill Livingstone, 1980.

3. Pirila V. Contact test versus patch test for epicutaneous testing. Contact Dermatitis, 1975; 1:48-52.

4. Cronin, E. Contact Dermatitis. New York: Churchhill Livingstone, 1980.

5. Wilkinson, D.S., Fregert, S., Magnusson, B. et al, Terminology of contact dermatitis. Acta Dermato-venereologica, 1970; 50:287-292.

6. Rosner, B. Fundamentals of Biostatistics. Boston: Duxbury Press, 1982.

7. Mantel, N. Chi-square test with one degree of freedom; extensions of the Mantel-Haenszel procedure. J. of the Amer. Stat. Assoc., 1963; 58:690-700.

8. Silberman, D.E., Sorrell, A.H. Allergy in fur workers with special reference to paraphenylenediamine. J. of Allergy, 1959; 30:11-18.

9. Knowles, F.C. Dermatitis caused by cosmetics and wearing apparel, particularly those containing paraphenylene diamin. Tr. Coll. Phys., Phila. 1916, S.3; 38:151-157.

10. Kilpikari, I. Occupational contact dermatitis among rubber workers. Contact Dermatitis, 1982; 8:359-362.

11. Calnan, C.D. Dermatology and industry, Clinical and Experimental Dermatology, 1978; 3:1-16.

12. Jordan, W.P. Jr. Contact dermatitis from N-isopropyl-n-phenyl paraphenylenediamine: "Volkswagen dermatitis." Arch. of Dermatology, 1971; 103:85-87.

13. Vestey, J.P., Buxton, P.K., Savin, J.A. Eyelash curler dermatitis. Contact Dermatitis, 1985; 13(4):274-275.

14. Curtis, G.H. Contact dermatitis of eyelids caused by an anti-oxidant in rubber fillers of eyelash curlers. Arch. of Dermatol., 1945; 52:262-265.

15. Fowler, J.F. Jr. Occupational dermatitis from stamp pad ink. Contact Dermatitis, 1987; 16(1):38.
16. Cronin, E. Contact Dermatitis. New York: Churchhill Livingstone, 1980.

17. Lynde, C.W., Mitchell, J.C. Patch test results in 66 hairdressers 1973-81. Contact Dermatitis, 1982; 8:302-307.

18. Marzulli, F.W., Maibach, H.I. The use of graded concentrations in studying skin sensitizers: Experimental contact sensitization in man. Food and Cosmetics Toxicology, 1974; 12:219-227.

19. Fisher, A.A. Contact Dermatitis, 3rd Ed., Philadelphia: Lea & Febiger, 1986:37.

20. Kligman, A. The identification of contact allergens by human assay. J. Invest. Dermatol., 1966; 47:393-409.

21. Thyresson, N., Skog, E. Occupational dermatoses among panel patients. Acta Dermatologica - Venereologica, 1953; 33(6):463-470.

22. Cosmetic Injury Reports. FY Filed in Division of Cosmetics Technology, Bureau of Foods, Food and Drug Administration, Washington, D.C., 1974.

23. Fisher, A.A. Contact Dermatitis, 3rd Ed., Philadelphia: Lea & Febiger, l986:37.

24. Garfinkel, J., Selvin, S. and Brown, S.M. Possible increased risk of lung cancer among beauticians. J. Nat. Cancer Inst., l977; 58:l4l-l43.

25. Kinlen, L.J. et al, Use of hair dyes by patients with breast cancer: a case-control study. Brit. Med. Jour., l977; 2:366-368.

26. Menck, H.R. et al Lung cancer risk among beauticians and other female workers. J. Nat. Cancer Inst., l977; 59(2):l423-l425.

27. Shafer, N., Shafer, R.W. Potential of carcinogenic effects of hair dyes. New York State J. of Med., l976; 76:394-396.

28. Hennekens, C.H. et al, Use of permanent hair dyes and cancer among registered nurses. Lancet, l979; l(8l3l):l390-l393.

29. National Institute for Occupational Safety and Health. Current intelligence bulletin l9–2,4,-diaminoanisole (4-methoxy-m-phenylenediamine) in hair and fur dyes. Cincinnati, Ohio: National Institute for Occupational Safety and Health, l978. (DHHS (NIOSH) publication no. 78-111).

30. Hanzlik, P.J. The pharmacology of some paraphenylenediamines. J. Ind. Hygiene, l923; 4:386-407.

3l. National Institute for Occupational Safety and Health, Registry of Toxic Effects of Chemical Substances, l983 Supplement. Cincinnati, Ohio: National Institute for Occupational Safety and Health, l983.

32. Nat. Academy of Sciences, Nat. Research Council, Chemical-Biological Coordination Center, Review, Washington, D.C. l953; 5: ll.

33. Nat. Academy of Sciences, Nat. Research Council, Chemical-Biological Coordination Center, Review, Washington, D.C. l953; 5:ll.

34. Progress Report for Contract No. NIH-NCI-E-C-72-3252. Submitted to the National Cancer Institute by Litton Bionetics, Inc. (Bethesda, Md.)

35. Some Aromatic Amines and Related Nitro Compounds - Hair Dyes, Colouring Agents and Miscellaneous Industrial Chemicals, International Agency for Research on Cancer (IARC), World Health Organization, Lyon, France, Jan. l978; l6:l25-l42.

36. Bioassay of p-Phenylenediamine Dihydrochloride for Possible Carcinogenicity, NCI Carcinogenesis Technical Report Series No. l74, l979 CAS No. 624-l8-0, NCI - CG-TR-l74, U.S. DHHS, PHS, NIH.

37. Dieke, S.H., Allen G.S., and Richter C.P. The acute toxicity of thioureas and related compounds to wild and domestic Norway rats. J. of Pharmacology & Experimental Therapeutics, May, l977; 90:260-270.

38. Davies, R.E., Harper, K.H. and Kynoch, S.R. Inter-species variation in dermal reactivity. J. of the Soc. of Cosmetic Chemists, l972; 23:37l-381.

39. Burnett, C., Loehr, R., Corbett, J. Dominant lethal mutagenicity study on hair dyes. J. of Toxicology and Environmental Health, l977; 2:657-662.

40. Hanzlik, P.J. The pharmacology of some paraphenylenediamines. J. Ind. Hygiene, l923; 4:386-407.

4l. Hanzlik, P.J. The pharmacology of some paraphenylenediamines. J. Ind. Hygiene, l923; 4:386-407.

42. Hanzlik, P.J. The pharmacology of some paraphenylenediamines. J. Ind. Hygiene, l923; 4:386-407.

43. American Conference of Governmental Industries Hygienists. Documentation of the threshold limit values. 5th ed. Cincinnati, Ohio: ACGIH, l980.
44. Goldblatt, M.W. Research in industrial health in the chemical industry. Brit. J. Ind. Med., l955; l2:l-20.

45. Marks, R., Cronin, E. Hand eczema in hairdressers. Aust. J. Derm., l977; l8:l23-l26.

46. Barrett, J.T. Basic Immunology and its Medical Application, 2nd Ed., St. Louis: C.V. Mosby Co., l980.

47. Schlesselman, J.J. Case-Control Studies: Design, Conduct, Analysis. New York: Oxford University Press, l982.

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2. NIOSH, Atlanta Region
3. OSHA, Region IV

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TABLE l

DEMOGRAPHIC CHARACTERISTICS OF 99
QUESTIONNAIRE RESPONDENTS

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Mean Age	42.6 years	s.d. l2.8
Race	Number	Percent
Hispanic	24	24
Black	27	27
White	46	47
Other	2	2
Sex		
Male	3l	3l
Female	68	69

TABLE 2

THE RELATIVE RATES OF DERMATITIS AMONG LABORATORY WORKERS AT THE DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES LABORATORIES, FLORIDA

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

		Noncases and Cases	Cases	RR	X^2	C.I.*
Race						
	White	46	l6	l.00		
	Black	27	6	0.64	l.27	.29,l.40
	Hispanic	24	l2	l.44	l.52	.80,2.57
	Other	2	0	0	l.04	
Sex						
	Female	31	22	l.00		
	Male	68	12	l.20	.38	.68,2.12
Atopy	Yes	48	l7	l.06	.05	.6l,l.84
	No	5l	l7			
Eczema	Yes	8	3	l.l0	.04	.42,2.89
	No	9l	26			
Family History						
	Yes	l4	5	l.05	.0l	.48,2.26
	No	85	29			
Cleaner use						
	Yes	76	27	l.l7	.20	.59,2.30
	No	23	7			
Handwashing <l5/Day	Yes	5l	l9	l.l9	.40	.69,2.07
	No	48	l5			
Oxidase Exposed						
	Yes	54	24	2.00	5.38	1.11,3.60
	No	45	l0			
CO_2 Exposed						
	Yes	60	27	2.51	7.67	1.30,4.82
	No	39	7			

TABLE 2
(CONTINUED)

THE RELATIVE RATES OF DERMATITIS AMONG LABORATORY WORKERS AT THE DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES LABORATORIES, FLORIDA

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

*95% Confidence Intervals

Race = Comparisons use whites as the baseline.

Sex = Females as the baseline.

Atopy = Personal or family history of allergic rhinitis, asthma, or eczema.

Eczema = Individuals with a personal history of eczema.

Family History = Individuals with a family history of allergy.

Handwashing = Individuals washing their hands less than l5 times a day.

Cleaner = Individuals with personal use of laboratory countertop cleaners.

Oxidase Exposed = Individuals applying oxidase reagent.

CO_2 Exposed = Individuals handling plates from bags containing CO_2 generating tablets.

TABLE 3

PATCH TEST RESULTS OF SENSITIZED INDIVIDUALS**

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Patch Test Reagents*

Laboratory	l	2	3	4	5	6	7	8	9	l0	ll
Jacksonville											
Worker											
#1	3+	3+	3+	3+	-	1+	-	-	IR		
#2	3+	3+	3+	3+	-	-	-	-	IR		
Miami											
#3	3+	3+	3+	3+	-	-	-	-	2+	-	-
#4	2+	2+	2+	2+	-	-	-	-	-	IR	-
Tallahassee											
#5	3+	3+	3+	3+	-	1+	-	IR	-		
Tampa											
#6	2+	2+	2+	2+	-	-	-	-			
#7	2+	2+	2+	2+	-	-	-	-			

*Test Substances

l= Dimethyl-p-phenylenediamine oxalate l% in petrolatum from the Miami Laboratory.

2= Dimethyl-p-phenylenediamine oxalate l% in petrolatum from the Jacksonville Laboratory.

TABLE 3
(CONTINUED)

PATCH TEST RESULTS OF SENSITIZED INDIVIDUALS**

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

3 = N,N,N',N'-tetramethyl-p-phenylenediamine dihydrochloride l% in petrolatum from the Orlando Laboratory.

4 = N,N-dimethyl-p-phenylenediamine monohydrochloride l% in petrolatum from the Cincinnati Health Department Laboratory.

5 = Carbon Dioxide (CO_2) generating tablet, l0% in petrolatum (consists of 50% NaH_2CO_3, 20% Citric Acid, 20% Micro-C-Cellulose, 8.5% Glycol, l.5% Talc).

6 = Paraphenylenediamine, l% in petrolatum from standard dermatological test tray.

7 = Blank petrolatum.

8 = 2% Staphene at Jacksonville Laboratory; paraphenylenediamine, l% in petrolatum at the Miami Laboratory; 30% Staphene (consists of 5.57% potassium o-benzyl p-chlorophenate, 5.52% potassium p-tertiary amylphenate, 5.5l% potassium o-phenyl-phenate, and 83.4% inert ingredients) at the Tallahassee Laboratory; and 5% Staphene at the Tampa Laboratory.

9 = Vestal soap, full strength at the Jacksonville Laboratory; Septisol, 5% at the Miami Laboratory; 5% Amphyl at the Tallahassee Laboratory.

l0 = Staphene, 5% at the Miami Laboratory.

ll = Perfumed Liquid Soap, full strength, at the Miami Laboratory.

** Interpretation of Skin Patch Test Results:

- = no reaction or negative.

l+ = weak, non-vesicular reaction.

2+ = strong, an edematous, vesicular reaction.

3+ = extreme, a bullous or ulcerative reaction.

IR = an irritant skin reaction.

TABLE 4
RISK FACTORS FOR DERMATITIS
(SENSITIZED AND NONSENSITIZED CONTACT DERMATITIS)
AMONG WORKERS AT THE DEPARTMENT OF HEALTH
AND REHABILITATIVE SERVICES LABORATORIES, FLORIDA*
FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

TABLE 4a: Risk of Being a Sensitized Case

		Noncases + Sensitized Cases	Sensitized Cases	RR	C.I.
Race					
	White	34	4	l.00	
	Black	22	l	.39	0.05,2.95
	Hispanic	l4	2	l.2l	0.25,6.02
	Other	2	0	0	
Sex					
	Females	23	4	2.84	0.72,ll.7
	Males	49	3	l.00	
Atopy	Yes	33	2	.47	0.l0, 2.l9
	No	39	5		
Family History					
	Yes	9	0	0	
	No	63	7		
Eczema	Yes	6	l	l.83	0.25,l3.5
	No	66	6		
Cleaners					
	Yes	56	7	Undef.	
	No	l6	0		
Handwashing					
<l5/Day	Yes	38	6	5.37	0.88,32.7
	No	34	l		
Oxidase Exposed					
	Yes	37	7	Undef.	
	No	35	0		
CO_2 Exposed					
	Yes	40	7	Undef.	
	No	32	0		

TABLE 4
(CONTINUED)

RISK FACTORS FOR DERMATITIS
(SENSITIZED AND NONSENSITIZED CONTACT DERMATITIS)
AMONG WORKERS AT THE DEPARTMENT OF HEALTH
AND REHABILITATIVE SERVICES LABORATORIES, FLORIDA*

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

TABLE 4a: Risk of Being a Sensitized Case

Race = Comparisons use whites as the baseline.

Sex = Females as baseline.

Atopy = Personal or family history of asthma, allergic rhinitis or eczema.

Family History = Family history of allergy.

Eczema = Personal history of eczema.

Cleaners = Personal use of laboratory countertop cleaners.

Handwashing = Individuals washing their hands less than l5 times a day.

Oxidase Exposed = Individuals applying oxidase reagent.

CO_2 Exposed = Individuals handling plates from plastic bags containing CO_2 generating tablets.

* Comparisons in this table assume all sensitized individuals were among the patch test positive cases.

** 95% Confidence Intervals.

TABLE 4

POTENTIAL RISK FACTORS FOR DERMATITIS
(SENSITIZED AND NONSENSITIZED CONTACT DERMATITIS)
AMONG WORKERS AT THE DEPARTMENT OF HEALTH
AND REHABILITATIVE SERVICES LABORATORIES, FLORIDA*

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

TABLE 4b: Risk of Being a Non-sensitized Case

		Noncases + Non-sensitized Cases	Non-sensitized Cases	RR	C.I.**
Race					
	White	42	l2	l.00	
	Black	26	5	.67	0.27,l.66
	Hispanic	22	l0	l.59	0.8l,3.l4
	Other	2	0		
Sex					
	Females	65	19	l.00	
	Males	27	8	l.01	0.52,1.99
Atopy	Yes	46	l5	l.25	0.66,2.37
	No	46	l2		
Family History					
	Yes	l4	5	l.27	0.56,2.87
	No	78	22		
Eczema	Yes	8	3	l.3l	0.48,3.6l
	No	84	24		
Cleaners	Yes	69	20	.95	0.46,l.97
	No	23	7		
Handwashing <l5/Day	Yes	45	l3	.97	0.5l,l.83
	No	47	l4		
Oxidase Exposed					
	Yes	47	l7	l.63	0.85,3.l3
	No	45	l0		
CO_2 Exposed					
	Yes	52	l9	l.83	0.92,3.63
	No	40	8		

TABLE 4
(CONTINUED)

POTENTIAL RISK FACTORS FOR DERMATITIS
(SENSITIZED AND NONSENSITIZED CONTACT DERMATITIS)
AMONG WORKERS AT THE DEPARTMENT OF HEALTH
AND REHABILITATIVE SERVICES LABORATORIES, FLORIDA*

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Race = Comparisons use whites as the baseline.

Sex = Females as baseline.

Atopy = Personal or family history of asthma, allergic rhinitis or eczema.

Family History = Family history of allergy.

Eczema = Personal history of eczema.

Cleaners = Personal use of laboratory countertop cleaners.

Handwashing = Individuals washing their hands less than l5 times a day.

Oxidase Exposed = Individuals applying oxidase reagent.

CO_2 Exposed = Individuals handling plates from plastic bags containing CO_2 generating tablets.

* Comparisons in this table assume all sensitized individuals were among the patch test positive cases.
** 95% Confidence Intervals.

TABLE 5
EFFECT MODIFICATION BETWEEN EXPOSURE TO OXIDASE REAGENT
AND OTHER RISK FACTORS AND THE RISK OF IRRITANT DERMATITIS*
FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA / HETA 87-042 / JANUARY l987

		Risk Factor +				Risk Factor -			
Oxidase Exposurel.		Atopy +		RR	C.I.	Atopy -		RR	C.I.**
		Case	Noncase			Case	Noncase		
	+	8	l5	l.65	.60,4.56	9	l5	l.39	.6l,3.l6
	-	4	l5			7	l9		
2.		Family History +				Family History -			
		Case	Noncase			Case	Noncase		
	+	3	4	l.50	.34,6.58	l4	26	l.66	.80,3.46
	-	2	5			8	30		
3.		Eczema +				Eczema -			
		Case	Noncase			Case	Noncase		
	+	3	2	Undef.		l4	28	l.27	.66,2.47
	-	0	3			ll	3l		
4.		Cleaners +				Cleaners -			
		Case	Noncase			Case	Noncase		
	+	l5	28	l.74	.75,4.06	2	2	l.67	.45,6.24
	-	5	20			6	l4		
5.		Handwashing +				Handwashing -			
		Case	Noncase			Case	Noncase		
	+	8	l7	l.l7	.42,2.87	9	l3	2.35	.89,6.23
	-	6	l6			4	l9		

* sensitized cases are excluded.
** 95% Confidence Intervals.

Atopy = personal history of seasonal rhinitis, asthma or eczema.
Family History = family history of allergy.
Eczema = personal history of eczema.
Cleaners = use of laboratory countertop cleaners.
Handwashing = individuals washing their hands at least l5 times a day.

TABLE 6

AVERAGE WORKER EXPOSURE ESTIMATES TO OXIDASE REAGENTS
AND CARBON DIOXIDE GENERATING TABLETS*

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

	Noncases	All Cases	Sensitized Cases	Non-Sensitized Cases
MOSOX	51.6	58.9	87.0	51.7
OXPLATWK	1,107	1,012	1,393	913
OXDOSE	253,613	352,194	719,411	256,990
MOSCO2	60.1	32.4	27.4	33.7
COPLATWK	810	931	1,482	787
CO2DOSE	217,315	205,798	156,161	218,667

* Only workers exposed to the oxidase reagent or CO_2-generating tablets were used to calculate the average estimates of exposure.

MOSOX = Total months workers applied oxidase reagent to culture plates.

OXPLATWK = Average number of culture plates to which oxidase is applied per week.

OXDOSE = OXPLATWK X Total number of weeks oxidase is applied to culture plates.

MOSCO2 = Total months workers handled culture plates from plastic bags containing CO_2 generating tablets.

COPLATWK = Average number of culture plates per week handled from plastic bags containing CO_2 generating tablets.

CO2DOSE = COPLATWK X Total number of weeks culture plates were handled from plastic bags containing CO_2 generating tablets.

TABLE 7

RELATIVE RISK OF DERMATITIS BY LEVEL OF EXPOSURE

(X^2 TEST FOR TREND OVER EQUAL DOSAGE INTERVALS
OF OXIDASE EXPOSURE, USING ALL CASES AND NONCASES*)

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Interval (Log_0)	Level of Exposure (Log_0 of Interval Mean)	Cases	Noncases	RR	C.I.**
	0	10	35	1.00	
2.ll-3.24	2.72	1	3	1.13	.l8,6.96
3.25-4.38	3.87	5	10	1.50	.59,3.8l
4.39-5.52	4.97	12	8	2.70	l.39,5.23
5.53-6.66	6.03	6	6	2.25	.97,5.23
Total		34	62		

X^2=7.94, l d.f., p<.005

*3 noncases were excluded from the analysis due to inadequate data to calculate their exposure. Logarithmic transformation was performed on the exposure variable, number of culture plates processed, used as a proxy for oxidase exposure.

** 95% Confidence Intervals.

TABLE 8

RELATIVE RISK OF DERMATITIS BY LEVEL OF EXPOSURE

(X^2 TEST FOR TREND BY EQUAL DISTRIBUTION OF CASES
AND NONCASES OVER THE DOSAGE RANGE
OF OXIDASE EXPOSURE, USING ALL CASES AND NONCASES*)

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Interval (Log_{10})	Level of Exposure (Log_{10} of Interval Mean)	Cases	Noncases	RR	C.I.**
	0	l0	35	l.00	
2.ll-4.0l	3.38	3	l0	l.04	.33,3.22
4.02-4.74	4.39	7	6	2.42	l.l0,5.36
4.74-5.53	5.l9	8	5	2.77	l.3l,5.84
5.54-6.63	6.03	6	6	2.25	.97,5.23
Total		34	62		

X_2=8.24, l d.f., p<.005

*3 noncases were excluded from the analysis due to inadequate data to calculate their exposure. Logarithmic transformation was performed on the exposure variable, number of culture plates processed, used as a proxy for oxidase exposure.

**95% Confidence Intervals

TABLE 9

RELATIVE RISK OF DERMATITIS BY LEVEL OF EXPOSURE

(X^2 TEST FOR TREND OVER EQUAL DOSAGE INTERVALS
OF OXIDASE EXPOSURE USING
NON-SENSITIZED CASES AND NONCASES*)

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Interval (Log_{10})	Level of Exposure (Log_{10} of Interval Mean)	Non-sensitized Cases	Noncases	RR	C.I.**
	0	l0	35	l.00	
2.ll-3.l6	2.56	1	2	1.50	.25,9.l7
3.l7-4.23	3.79	4	l0	l.29	.46,3.56
4.24-5.28	4.67	3	7	l.35	.43,4.l9
5.29-6.34	5.80	9	8	2.38	l.l4,4.96
Total		27	62		

X^2=3.94, l d.f., p<.05

*3 noncases were excluded from the analysis due to inadequate data to calculate their exposure, and all sensitized cases were also excluded. Logarithmic transformation was performed on the exposure variable, number of culture plates processed, used as a proxy for oxidase exposure.

** 95% Confidence Intervals

TABLE l0
RELATIVE RISK OF DERMATITIS BY LEVEL OF EXPOSURE
(X^2 TEST FOR TREND BY EQUAL DISTRIBUTION OF
CASES AND NONCASES OVER THE DOSAGE INTERVALS OF OXIDASE EXPOSURE,
USING NON-SENSITIZED CASES AND NONCASES*)
FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042
JANUARY l987

Interval (Log_{0})	Level of Exposure (Log_{0} of Interval Mean)	Non-sensitized Cases	Noncases	RR	C.I.**
	0	l0	35	l.00	
2.ll-3.94	3.27	2	9	.82	.2l,3.l7
3.95-4.59	4.3l	5	7	l.87	.75,4.68
4.60-5.5l	5.l5	5	5	2.25	.92,5.53
5.52-6.34	5.98	5	6	2.05	.83,5.07
Total		27	62		

X^2=4.l3, l d.f., p<.05

*3 noncases were excluded from the analysis due to inadequate data to calculate their exposure, and all sensitized cases were also excluded. Logarithmic transformation was performed on the exposure variable, number of culture plates processed, used as a proxy for oxidase exposure.

** 95% Confidence Intervals

TABLE ll
RELATIVE RISK OF SENSITIZATION BY LEVEL OF EXPOSURE
(X^2 TEST FOR TREND OVER EQUAL DOSAGE INTERVALS
OF OXIDASE EXPOSURE, USING SENSITIZED
CASES AND NONCASES*)
FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042
JANUARY l987

Interval Range (Log_{0})	Level of Exposure (Log_{0} of Interval Mean	Oxidase Sensitized Cases	Exposed Noncases	RR	C.I.**
.0l-4.37	3.59	l	l3	l.00	
4.38-6.63	5.35	6	l4	4.20	.72,24.4
Total		7	27		

X^2=l0.67, l d.f., p<.005

*3 noncases were excluded from the analysis due to inadequate data to calculate their exposure, and all non-sensitized cases were also excluded. All nonexposed non-cases were assumed to be non-sensitized, although this was not confirmed by patch testing. Logarithmic transformation was performed on the exposure variable, number of culture plates processed, used as a proxy for oxidase exposure.

** 95% Confidence Interval.

TABLE l2

RELATIVE RISK OF SENSITIZATION BY LEVEL OF EXPOSURE

(X^2 TEST FOR TREND BY EQUAL DISTRIBUTION OF CASES AND NONCASES OVER THE DOSAGE INTERVALS OF OXIDASE EXPOSURE, USING SENSITIZED CASES AND NONCASES*)

FLORIDA DEPARTMENT OF HEALTH AND REHABILITATIVE SERVICES
STATE OF FLORIDA
HETA 87-042

JANUARY l987

Interval Range (Log_{0})	Level of Exposure (Log_{0} of Interval Mean)	Oxidase Sensitized Cases	Exposed Noncases	RR	C.I.**
.01-4.60	3.76	l	l6	l.00	
4.6l-6.63	5.49	6	ll	6.00	l.l2,32.2
Total		7	27		

X_2=ll.76, l d.f., p<.005

*3 Noncases were excluded from the analysis due to inadequate data to calculate their exposure, and all non-sensitized cases were also excluded. All nonexposed noncases were assumed to be non-sensitized, although this was not confirmed by patch testing. Logarithmic transformation was performed on the exposure variable, number of culture plates processed, used as a proxy for oxidase exposure.

** 95% Confidence Interval.

APPENDIX: SURVEY QUESTIONNAIRE

FLORIDA STATE HEALTH DEPARTMENTS
HE: 87-042

IDENTIFICATION NUMBER:(leave blank for administrative purposes) /_/_/_/

LABORATORY LOCATION (CITY)_____

TODAY'S DATE (Month/Day/Year) /_/_/-/_/_/-/_/_/

PERSONAL IDENTIFICATION

PLEASE PRINT USING CAPITAL LETTERS

1. NAME (Last): _____
(First): _____
(Middle Initial): __

2. ADDRESS (Street): _____

(City): _____

(State): _____

(Zipcode) _____

3. TELEPHONE (Home) (Area Code) /_/_/_/-/_/_/_/-/_/_/_/_/

(Work) (Area Code) /_/_/_/-/_/_/_/-/_/_/_/_/

4. DATE OF BIRTH (Month/Day/Year): /_/_/-/_/_/-/_/_/

5. SEX: _MALE _FEMALE

6. RACE: _HISPANIC _ORIENTAL _BLACK _WHITE _OTHER

MEDICAL HISTORY

7. SINCE JANUARY 1, 1986 (WITHIN THE PAST YEAR), HAVE YOU HAD ANY OF THE FOLLOWING SKIN CONDITIONS? (*IF NO, SKIP TO QUESTION 13)

PLEASE CIRCLE THE BEST ANSWER

1. Red bumps, blotches or other rashes lasting one or more days

2. Excessive dryness and/or chapping only lasting one or more days

3. Itching of skin only, lasting one or more days (no visible skin changes)

4. Other (Describe)_____

8. PLEASE INDICATE ON WHAT PART(S) OF YOUR BODY YOU HAVE BEEN EXPERIENCING THIS RASH OR SKIN CONDITION.
(CIRCLE ALL AREAS THAT APPLY).

1.scalp 7.stomach 13.feet

2.eyelids 8.upper arms 14.groin

3.face 9.elbows 15.buttocks

4.neck 10.elbow creases 16.hands
a. backs of hands

5.back 11.lower arms
b. palms of hands

6.chest 12.legs
c. fingers

19.Other (Describe)_____

9. WHEN DID THESE SYMPTOMS OR CHANGES IN YOUR SKIN FIRST BEGIN?

(month/day/year) /_/_/-/_/_/-/_/_/

10. HAS THE SKIN CONDITION COMPLETELY DISAPPEARED OR RESOLVED?

yes no don't know

11. HAS YOUR SKIN CONDITION IMPROVED OR DISAPPEARED DURING ANY OF THE FOLLOWING TIMES, AWAY FROM YOUR JOB, LISTED BELOW?

yes no don't know

IF YES, CIRCLE ALL TIMES BELOW THAT APPLY.

a. weekends or days off
b. vacation
c. medical or sick leave
d. lay-off
e. job or work area change
f. other (Describe)_____

12. DO YOU BELIEVE YOUR SKIN RASH OR SKIN CONDITION HAS BEEN CAUSED BY ANYTHING TO WHICH YOU HAVE BEEN EXPOSED WHILE WORKING AT THE STATE HEALTH LABORATORY?

yes no don't know

If "yes", specify_____

13. HAVE YOU EVER DYED OR COLORED YOUR HAIR?

yes no don't know

IF "YES", DID THE HAIR DYE OR COLORING AGENT EVER CAUSE A SKIN REACTION?

yes no don't know

Please specify product used if known _____

14. HAVE YOU EVER HAD ITCHY, WATERY EYES OR RUNNY, STUFFY NOSE IN THE ABSENCE OF COLDS OR "FLU," WHEN AROUND FLOWERS, TREES, RAGWEED, FEATHERS, OR ANIMALS?

yes no don't know

15. HAVE YOU EVER HAD PROLONGED COUGHING, WHEEZING, OR DIFFICULTY BREATHING, IN THE ABSENCE OF COLD OR "FLU," WHEN AROUND FLOWERS, TREES, RAGWEED, FEATHERS, OR ANIMALS?

yes no don't know

16. HAVE YOU EVER HAD SKIN RASHES IN THE CREASES OF THE ELBOWS OR BEHIND THE KNEES, AS A CHILD OR TEENAGER?

yes no don't know

17. HAVE YOUR PARENTS, BROTHERS, OR SISTERS HAD ANY OF THE THREE CONDITIONS MENTIONED IN QUESTIONS 14, 15, OR 16?

yes no don't know

WORK HISTORY

18. PLEASE ENTER YOUR JOB CLASSIFICATION OR TITLE _____

19. ESTIMATE THE AMOUNT OF TIME YOU HAVE WORKED AT THE STATE HEALTH DEPARTMENT LABORATORY?

YEARS___ MONTHS___

20. PLEASE ESTIMATE THE NUMBER OF TIMES YOU WASH YOUR HANDS IN A TYPICAL WORKDAY.

NUMBER OF TIMES _____

21. DO YOUR WORK DUTIES USUALLY INCLUDE THE CLEANING OF LABORATORY COUNTERTOPS WITH DISINFECTANT?

yes no don't know

22. SINCE YOU HAVE WORKED IN THE STATE HEALTH DEPARTMENT, HAVE YOU HELPED IN THE PROCESSING OF GC (GONORRHEA) CULTURE PLATES?**

yes no don't know

**A yes answer would include duties such as plating, transporting, incubating, applying oxidase reagent, gramstaining, processing GC lab slips, etc.

IF YOU ANSWERED YES TO QUESTION 22, PLEASE COMPLETE QUESTIONS 23 THROUGH 26.

IF YOU ANSWERED NO TO QUESTION 22, PLEASE GO TO THE BOTTOM OF THE LAST PAGE.

23. ESTIMATE THE AVERAGE NUMBER OF DAYS IN YOUR WORKWEEK THAT ARE/WERE USED FOR PROCESSING GC PLATES.

(if you have had a change in assignment within the last year, or are now rotating through different jobs in the lab, please refer to the time period you actually processed GC plates)

a. less than 1 day per week
b. 1 day per week
c. 2 days per week
d. 3 days per week
e. 4 days per week
f. 5 days per week
g. more than 5 days per week

24. IF YOU HAVE HAD DIRECT CONTACT WITH THE GC CULTURE PLATES, PLEASE ESTIMATE THE AVERAGE NUMBER OF PLATES YOU HANDLE(D) IN A TYPICAL DAY (Enter "0" if no direct contact).

(if you have had a change in assignment within the last year, or are now rotating through different jobs in the lab, please refer to the time period you actually processed GC plates)

NUMBER OF PLATES ____

25. HAVE YOU APPLIED OXIDASE REAGENT TO THE GC CULTURE PLATES?

yes no don't know

If YES,

A. estimate the average number of plates you applied oxidase reagent to in a typical day,

NUMBER OF PLATES ____

B. and the number of days per week you applied oxidase reagent to the GC culture plates.

a. less than 1 day per week
b. 1 day per week
c. 2 days per week
d. 3 days per week
e. 4 days per week
f. 5 days per week
g. more than 5 days per week

26. HAVE YOUR DUTIES REQUIRED YOU TO REMOVE GC CULTURE PLATES OR LAB SLIPS FROM PLASTIC BAGS WHICH ALSO CONTAINED CARBON DIOXIDE (CO_2) GENERATING TABLETS

yes no don't know

If YES,

A. estimate the number of bags handled per day,

NUMBER OF BAGS ____

B. and the number of days per week you handled the bags.

a. less than 1 day per week
b. 1 day per week
c. 2 days per week
d. 3 days per week
e. 4 days per week
f. 5 days per week
g. more than 5 days per week

THANK YOU

PLEASE FEEL FREE TO MAKE ANY COMMENTS OR EXPRESS ANY CONCERNS YOU MAY HAVE REGARDING YOUR WORK WITH THE GC CULTURE PLATES IN THE LABORATORY AND RELATED SKIN OR HEALTH PROBLEMS.

APPENDIX II

NAME_____(please print)

l. HAVE YOU EVER WORKED WITH THE OXIDASE REAGENT IN THE PAST?

YES NO

IF YES, PLEASE ENTER THE TOTAL NUMBER OF MONTHS AND/OR YEARS

YOU HAVE WORKED WITH OXIDASE REAGENT.

MONTHS ____ YEARS ____

ALSO ENTER THE NUMBER OF MONTHS YOU HAVE WORKED WITH OXIDASE

REAGENT IN THE LAST YEAR (l986).

MONTHS ____

2. HAVE YOU EVER HANDLED THE BAGS CONTAINING THE GONORRHEA

CULTURE PLATES AND CO_2 PILLS?

YES NO

IF YES, PLEASE ENTER THE TOTAL NUMBER OF MONTHS AND/OR YEARS

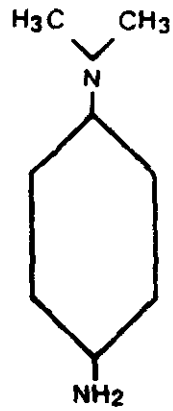
YOU HAVE WORKED WITH THE BAGS CONTAINING CULTURE PLATES AND CO_2 PILLS.

MONTHS ____ YEARS____

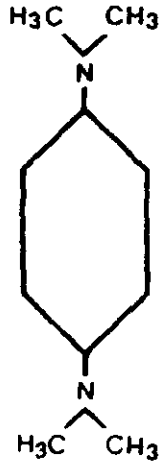
ALSO ENTER THE NUMBER OF MONTHS YOU HAVE WORKED HANDLING THE BAGS

CONTAINING PLATES AND CO_2 PILLS IN THE LAST YEAR (l986).

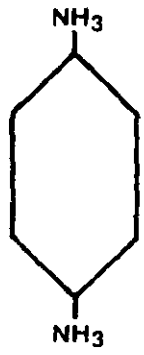
MONTHS ____



N,N Dimethyl – paraphenylenediamine (DMPPD)
or p – aminodimethyl – aniline



N,N,N',N' Tetramethyl – p – phenylenediamine (TMPPD)



p – Phenylenediamine (PPD) or (p – Diaminobenzene)

Figure 1: p-phenylenediamine and two closely related chemical derivatives known as oxidase reagents.