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Deployment as a Risk Factor for a Positive PPD Reaction in Air Mobility Command

by

Margaret Kitt Herrick

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Abstract

Deployment as a Risk Factor for a Positive PPD Reaction in Air Mobility Command

by Margaret Kitt Herrick

Chairperson of the Supervisory Committee: Professor Hjordis M. Foy
Epidemiology

Current guidelines for tuberculosis (TB) testing in the Air Force are defined in Air Force Instruction (AFI) 48-115. Secondary to increased participation in overseas operations, Air Mobility Command (AMC) instituted a new policy in 1995. In addition to those tested in accordance with the above AFI, annual testing is now required for all individuals on flying status, mobility, or with a high potential for overseas travel.

The purpose of this case-control study was to assess the risk of overseas deployment and assignment for development of a positive PPD reaction. Demographics of PPD positive and negative Air Force personnel were described. The target population was active duty personnel in AMC. Information was collected from three of eleven AMC bases. Cases were personnel identified as PPD positive when tested during calendar year 1995. Controls were randomly chosen from personnel testing PPD negative in 1995. They were selected from the same three bases proportional to the number of cases obtained at a given location.

When gender and assignment to a medical unit were controlled as confounding variables, nonflyers who deployed overseas were at an increased risk for tuberculosis infection. However, the risk was not as strong as anticipated. A significant association

was not identified for flyers. Over fifty percent of personnel who tested positive for TB had not been deployed or assigned overseas. These individuals would not have been detected if not for their mobility status.

Until better risk identification is available for Air Force personnel, Air Mobility Command's policy of routine testing for all flyers and mobility personnel is justified.

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DEDICATION

To Brad, for all his encouragement and support.

BACKGROUND

Tuberculosis (TB) is the leading cause of death from any single infectious agent.[1] TB skin testing is the principal tool for control of this disease. The test identifies infected individuals. who are often asymptomatic, through a delayed cellular hypersensitivity reaction to tuberculin.[2] Infected individuals can be given prophylactic treatment with antibiotics to prevent progression to active disease. This preventive action decreases morbidity and reduces further disease transmission. The single most specific and sensitive screening test used is the Purified Protein Derivative (PPD) skin test, Mantoux Method. The Centers for Disease Control (CDC) recommend clinicians make PPD testing part of their routine evaluation of patients who fall into high risk groups.[3]

The incidence of active tuberculosis is generally lower for Active Duty Air Force (ADAF) personnel than for the general U.S. population.[4] Most Air Force members do not belong to high risk groups, but recent participation in overseas operations in regions with a high prevalence of TB potentially increases the risk of exposure for many airmen. Deployment is defined as the temporary relocation of the force to any desired area of operation.[5] This differentiates from an overseas assignment which must be at least one year in duration. Flyers include pilots, navigators, flight engineers, loadmasters, and boom operators. They frequently travel to overseas locations, but rarely stay for an extended period of time. Unpredictable demands make it difficult to estimate the frequency of deployment for nonflyers. Some individuals rarely leave their base of assignment while other personnel are deployed several times per year.

In the mid 1980's, annual TB testing for all ADAF personnel ceased. According to Air Force policy, Air Force Instruction (AFI) 48-115,[6] TB skin testing is required for those entering Active Duty, personnel returning from an overseas assignment. individuals testing HIV positive, contacts of active TB patients, occupationally exposed personnel, Military Medical Treatment Facility personnel, and other high risk individuals. as defined by the Centers for Disease Control.[7]

In 1993, pre-and post-deployment TB tests were administered in response to an increasing number of overseas deployments. For logistical reasons, the success of this policy was marginal and very labor-intensive for public health technicians in the Air Force. Air Mobility Command (AMC), whose mission is global delivery of personnel and cargo, individually instituted a controversial policy in 1995. In addition to those covered by AFI 48-115, all flyers, personnel on mobility (defined as those individuals slotted to fulfill a specific war-time mission and possessing additional training, equipment. and medical preparedness to depart home station on short notice), and all others with high potential for overseas travel must be skin tested annually for TB. Although some public health officers believe this program is needed for adequate surveillance of airmen in AMC, others feel it provides excessive screening for a low risk group.

OBJECTIVE

The objective of this study was to measure the risk of PPD conversion with overseas deployment and/or assignment. Knowledge of this risk should contribute to the assessment and further development of TB preventive policies within AMC and the Air Force.

METHODS

This study began with the collection of available PPD testing information for ADAF members from all eleven AMC bases. This information was combined with a case-control study of overseas deployment and PPD conversion conducted at three of the eleven AMC bases.

PPD test data are collected annually from all eleven AMC bases and sent to AMC Headquarters. These reports contain the total number of people skin tested as well as the number of positive reactions per base. Bases did not record the total number of individuals tested until 1993. Since then, the calculation of the rates of PPD positivity per base and for all of AMC has been possible. The immunizations clinic at each base recorded all individuals tested in 1995 and their results. Positive and negative reactions were classified according to current CDC definitions.[8] A public health technician locally interviewed individuals with a positive test. The "Tuberculosis Detection and Control Data" form (AF Form 2453) was completed for all active duty individuals identified as PPD positive during 1995. These forms contained demographic information including age, gender, rank, flying status, unit (allowing occupation to be determined), date of present test and last negative skin test, classification as a positive reactor or recent converter, whether the person was placed on chemoprophylaxis, and if treatment was completed. Ethnicity was not documented on this form. Deployment and overseas assignment information were recorded in the medical record. A physician reviewed these data and further completed the forms during the individual appointments.

The case-control study was carried out at Dover, McChord, and Travis Air Force Bases. These three bases represented 40 percent of the AMC cases (253/631) for 1995. An incident case was defined as an individual, without prior history of a positive TB skin test, who had a positive PPD reaction in 1995. This included both recent converters and positive reactors. As defined in AFI 48-115,[9] converters were individuals under 35 years old who had, within a two year period, a 10mm or greater increase in induration to the PPD test. If individuals were 35 years or older, a 15mm or greater increase in induration defined a converter. Positive reactors were personnel with no previous test, an unknown date of previous test, or last known negative test greater than two years prior to current testing. The size of the reaction considered positive varied depending on the category of the person tested as described by the CDC.[10]

Excluded from this study were individuals found to be PPD positive upon entry to active duty, personnel identified as positive prior to relocation to the current AMC base, individuals with known exposure to an individual with active TB, and personnel for which no record was available. Individuals who were tested while still overseas, whether positive or negative, were not included in this study because their test results were not available in AMC records. Reasons for nonavailability of medical records included transfer to another base, separation or retirement from Active Duty, and current utilization by a clinic or provider.

Controls were defined as individuals who tested PPD negative in 1995. They were selected from the same three bases, proportional to the number of cases obtained from that

base. Personnel in immunization logs were numbered successively and then controls were selected using a random number table.[11] If the random number corresponded to a non-active duty member, an individual with a positive PPD test, a known contact of a person with active TB, or an individual no longer at that base, the number was omitted and the next number used. Retirement, separation from active duty, transfer to another base, and present deployment were the reasons individuals were no longer present at that base.

Demographic information for cases was obtained from "Tuberculosis Detection and Control Data" forms. Information on deployment and overseas assignment information since the last negative TB test was obtained from medical records. It was impossible to quantify short-duration overseas missions for flyers. Specific information was obtained for any trip where the individual remained in an overseas location for at least 14 days.

Demographic information for controls was obtained from computerized personnel files since "Tuberculosis Detection and Control Data" forms did not exist for them. Deployment and overseas assignment information between the last negative test and the 1995 test was obtained from the individuals via telephone contact. Availability of records was compared for cases and controls at McChord Air Force Base to assess this as a means of selection bias.

Epi Info 6.0 software was used for this bivariate analysis. Odds ratios (OR) were calculated using chi square statistics. For nonflyers, adjusted odds ratios were calculated

for gender and medical unit using the Mantel-Haenszel Method[12] to control for confounding.

RESULTS

Table 1 shows the number of positive PPD tests in ADAF in AMC obtained from the past three annual reports.[13,14,15] Although there has been an increase in both the number of positive PPD tests and the total number of tests administered in AMC, the rate of testing positive has changed little.

Table 2 summarizes characteristics of participants in the case-control study. The two groups were not significantly different in age or rank. The mean age of PPD positive subjects was 29.3 years and 27.7 years for PPD negative individuals. Cases were significantly more likely to be males than females. There was a high proportion of females in this study (15.4% of cases and 26.3% for controls) as compared to the 6.4% composition for the entire Air Force during 1995.[16]

The mean interval between PPD tests was 38.7 months for cases and 27.0 months for controls. When medical personnel were analyzed separately, these means decreased to 28.4 months for cases and 12.8 months for controls. Cases were significantly less likely than controls to have had a PPD test in the last 3 years (OR=0.56; 95% CI 0.35, 0.91). There was no significant difference between cases and controls when the interval between tests was 2 years or less. Individuals less than 35 years old were significantly more likely to have had a PPD test in the last 5 years compared to those 35 years or older (OR=2.85; 95% CI 1.48, 5.46).

Figure 1 shows that flyers were significantly more likely to be cases than controls (OR=3.04; 95% CI 1.43, 6.56). Medical personnel were significantly less likely to be

cases than controls (OR=0.29; 95% CI 0.15, 0.56). There was no significant difference between the two groups for any other unit of assignment.

Over half (50.3%) of the cases had neither deployed or been stationed overseas. Cases were over two times more likely to have been deployed between the last two TB tests than controls (OR=2.18; 95% CI 1.34, 3.54). Because flyers are likely to have shorter and more frequent deployments, better billeting conditions, and less social and working contact with local inhabitants, stratification by flying status was conducted to control for confounding (Table 3). In nonflyers, the risk of a positive PPD test with overseas deployment was 1.81 (95% CI 1.08, 3.02) when adjusted for medical unit and 2.10 (95% CI 1.28, 3.44) when adjusted for gender. This risk increased in nonflyers when the analysis included either an overseas assignment or deployment. The increased risk for flyers, in both instances, was not significant. In this study, there were no flyers assigned to medical units. Gender adjustment was not conducted for flyers due to an insufficient number of female flyers in the study. The risk associated with overseas assignment in nonflyers was 4.68 (95% CI 1.48, 14.78). The ability to assess the risk of overseas assignment in flyers was limited by the fact that only 2/49 flyers in this study had been assigned overseas.

When nonflyers (excluding medical personnel) were stratified according to the interval between TB tests, the risk of a positive PPD test associated with deployment was significant if the interval was $\leq$3 years (OR=2.32; 95% CI 1.12, 4.86) or $\leq$4 years

(OR=2.07; 95% CI 1.06, 4.05). There was no significant difference in risk for any other interval between TB tests.

For nonflyers who had been deployed, the frequency of deploying to more than one region in the interim between PPD tests was 39.3% (24/61) for cases and 9.8% (4/41) for controls (OR=6.0; 95% CI 1.73, 22.76). This increase in exposure strengthens the association between PPD conversion and deployment. There was no specific region that played a predominant role in risk and 12.2% of cases that had been deployed were in regions of Europe not considered high risk for TB. The reports for lengths of stay for deployments were not consistent in either group.

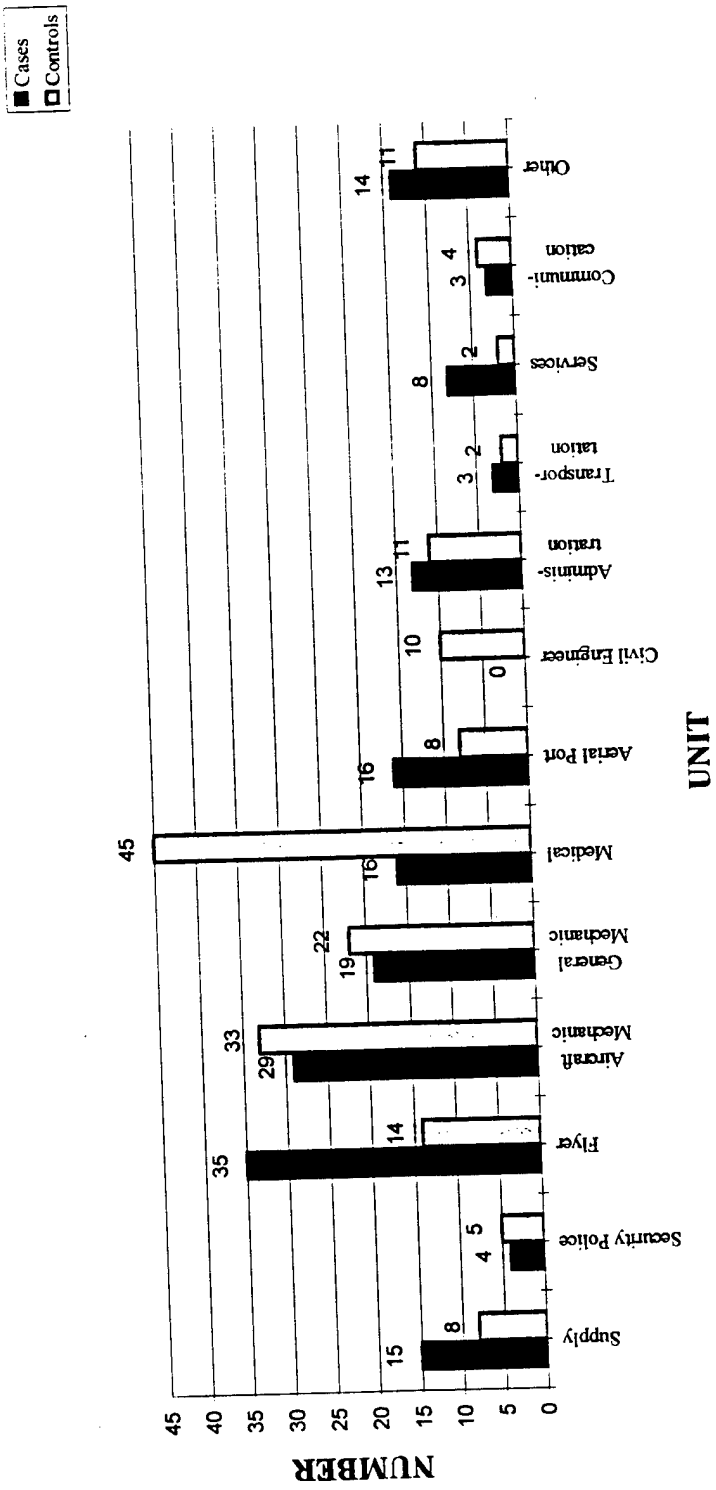

FIGURE 1: Unit of Assignment in Cases and Controls

TABLE 1: Rate of Positive PPD Tests in ADAF (AMC)

	# POSITIVE TESTS (REACTORS + CONVERTERS)	# TESTED	RATE
1993	226	6,262	36/1000
1994	271	10,235	26/1000
1995	631	24,636	26/1000

TABLE 2: Demographic Characteristics of Study Subjects According to PPD Status

	PPD + (n=175)		PPD - (n=175)		OR	95% CI
	#	%	#	%		
GENDER: Male	148	84.6	129	73.8	1.95	1.11-3.46*
AGE: <35	133	76.0	146	83.4	0.63	0.36-1.11
RANK: Enlisted	154	88.0	160	91.4	0.69	0.32-1.46
FLYER: Yes	35	20.0	14	8.0	2.67	1.33-5.39*
INTERVAL BETWEEN LAST TEST AND 1995 TEST:						
≤5 Yrs	135	77.1	157	89.7	0.39	0.20-0.73*
≤4 Yrs	118	67.4	149	85.1	0.36	0.21-0.63*
≤3 Yrs	106	60.6	128	73.1	0.56	0.35-0.91*
≤2 Yrs	90	51.4	104	59.4	0.72	0.46-1.13
≤1 Yr	47	26.9	39	22.3	1.28	0.76-2.15

* $p < 0.05$

TABLE 3: History of Overseas Travel in PPD Positive and PPD Negative Subjects

	Cases		Controls		Crude OR (95% CI)	Unit Adjusted[1] OR (95% CI)	Gender Adjusted OR (95% CI)
	#	%	#	%			
Deployment Flyers	13	37.1	3	21.4	2.17 (0.43-12.18)	--	--
Nonflyers	61	43.6	41	25.5	2.26 (1.34-3.81)[2]	1.81 (1.08-3.02)[2]	2.10 (1.28-3.44)[2]
Either Assignment OR Deployment Flyers	13	37.1	5	35.7	1.06 (0.24-4.74)	--	--
Nonflyers	74	52.9	45	28.0	2.89 (1.73-4.82)[2]	2.39 (1.45-3.94)[2]	2.72 (1.67-4.42)[2]

[1] Adjusted for Medical Unit
[2] $p < 0.05$

DISCUSSION

In the Air Force, there is a presumption that overseas deployment increases the risk of TB infection. This study confirmed an association between deployment and a positive PPD test in nonflyers. The risk was two to three times that of airmen that had not been deployed. A statistically significant association between deployment and a positive PPD test was not established for flyers, but the small number of flyers in the study precludes definitive conclusions.

The absence of a strong association between deployment and TB infection in nonflyers simply may reflect an insufficient sample size. An alternative explanation may be linked to the rate of TB infection in the United States during the study period. Positive PPD tests in the active duty population may be an extension of exposures here at home. U.S. epidemiological data suggest no single cause for this trend, but immigration and a rising prevalence of HIV infection are probable contributing factors for the general population. The CDC reports 71% of active TB cases in the U.S. in 1991 were in ethnic and racial minorities.[17] Unfortunately, this study could not analyze ethnicity as a variable.

In the case of flyers, deployment may have risks that are qualitatively different than nonflyers. All had traveled overseas extensively but lengths of stay were short compared to other groups in AMC. Arbitrarily defining deployment as a two week stay omitted potential exposures of shorter duration. Although the sample of flyers was small, this

study is consistent with earlier findings that flyers are less likely to become infected with TB than nonflyers.[18]

Confining this study to individuals tested and categorized within AMC limited the ability to assess the risk of overseas assignment within the Air Force. A broader analysis addressing the entire Air Force would better assess this aspect of risk. By definition, an overseas assignment is of longer duration than deployment. The increase in risk demonstrated when assignment was combined with deployment is consistent with the concept that increasing the duration of exposure is one factor that increases the likelihood TB will be transmitted to an individual.[19]

Limitations to this study include differences in exposure ascertainment between cases and controls. For a case to be included, the record had to be available. Overall, 69.2% of records were available for cases. In the comparison conducted at McChord Air Force Base, 71% of records were available for selected controls. For a control to be included, the individual had to be available. Retirement and separation accounted for the majority of exclusions in both cases and controls. Although an individual who is deployed frequently may be theoretically more likely to discontinue service, there is no reason to suspect that individuals who had separated or retired had different rates of deployment from their counterpart cases and controls. Recall bias for deployment information may have been present in favor of cases. However, deployment is a significant life event. In my contact with them, most controls went to great length to provide complete travel histories.

Improper technical method in administration or interpretation of the skin test could have resulted in false positive or false negative tests. Most immunization technicians undergo thorough training to minimize this occurrence. Transient, false positive reactions may have resulted from cross-reaction after exposures to other non-tuberculous mycobacteria.[20] Using an appropriate cut-off (<10mm) for categorization of a positive reaction minimizes this problem. Recent immunization with live virus vaccines such as measles, mumps, polio, and yellow fever could have lead to false negative tests.[21]

The study was restricted to a single year, when AMC policy was in transition. Policy may have been implemented to varying degrees.

The three bases selected for participation are probably representative of AMC. They maintain and fly similar aircraft and participate in comparable operations. The findings of this study may not be applicable to other Major Commands due to differences in the frequency of deployments and the extent to which squadrons deploy as cohesive units, often utilizing on-base temporary facilities.

The inclusion of medical personnel was originally felt to be acceptable due to the exclusion of both positive and negative individuals with known patient exposures. In this study, belonging to a medical unit gave the appearance of a protective effect against TB infection. This probably occurred for several reasons. Medical personnel in this study deployed less frequently (6.3% of cases and 2.2% of controls) than other nonflyers (48.4% of cases and 34.5% of controls). Medical personnel were also TB tested more frequently than other personnel. This increased their likelihood of being selected as a

control due to the volume of medical personnel tested, particularly at Travis Air Force Base, a regional medical center with several thousand employees. In medical units, 54.1% of individuals were female compared to 13.8% for non-medical units. This may have been a contributing factor to the differences in the distribution of females between cases and controls. The adjustments in the analysis are believed to have adequately corrected for this confounding.

Despite its limitations, this study has several implications for the TB testing policy of AMC. The fact that 50.3% of PPD positive individuals were neither deployed or assigned overseas is significant. These individuals had no other known reason for testing other than their mobility status. Their TB infection would most likely have gone undetected. This finding suggests we may be overlooking TB infection in our non-mobility personnel as well.

The risk of a positive PPD associated with deployment varied according to the interval between tests in nonflyers (excluding medical personnel). The larger number of cases without a test in the last 3 or more years, as compared to controls, suggests some of these individuals may have been infected years ago. This potential confounding may have caused an overestimation of their risk associated with recent deployments, compared with controls, who overall had been tested more frequently. Additionally, this delayed treatment is worrisome due to the increased risk of INH induced hepatitis in those over 35 years old. By increasing the frequency of testing, we will identify individuals closer to their initial time of infection, optimizing prophylactic treatment options.

At most AMC bases, the current system does not optimally capture personnel as they return from overseas deployments. Individuals who had been deployed to low-risk areas in Europe, would not even have been targeted for post-deployment testing. Multiple deployments may further increase risk, but these personnel are no less elusive to testing. Routine TB testing for mobility personnel, assures Air Force public health officials will at least identify these individuals.

This study suggests that although there is a risk of TB infection during deployment, other unidentified factors are involved. Since risks in these individuals are not clearly identified, the findings support current AMC testing policy. Until surveillance systems become better able to define and test high risk individuals, it may be prudent to have a more encompassing program. Cessation of annual testing for all Active Duty in the 1980's left many airmen with long intervals between tests. As "catching up" occurs for those on mobility, we may see a decreased number of new positive PPD tests. A similar analysis could then be repeated to determine if the risks, including deployment, can be more clearly delineated. At that point, adjustments in testing policy can be redressed. In this study there was no significant difference between cases and controls when the interval between tests was two years or less. It may reasonable to switch from annual testing to a 3 year testing policy, linked to other mobility immunization requirements.

These results provide an opportunity for further studies of the risk of TB infection in ADAF. Larger studies addressing flyers and medical personnel may provide better insight to risks associated with these individuals. However, a comment on data collection

is warranted. The present "Tuberculosis Detection and Control Data" form does not provide sufficient information to make this type of analysis routine. Expansion of the form to include overseas information, ethnicity, and applicable family history is necessary for better surveillance.

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APPENDIX A

Tuberculosis Detection and Control Data Form

TUBERCULOSIS DETECTION AND CONTROL DATA

(THIS FORM IS AFFECTED BY THE PRIVACY ACT OF 1974 - Use Blanket PAS DD Form 2005)

NAME OF PATIENT (Last, First, Middle Initial)	GRADE	SSAN	DOB	SEX
				MALE / FEMALE

STATUS	ORGANIZATION AND DUTY PHONE	HOME ADDRESS AND PHONE NO.
MILITARY / FLYING / CIVILIAN / FOREIGN NATIONAL / O-19		

NAME OF SPONSOR *(If patient is a dependent)*

SKIN TEST INFORMATION			CLASSIFICATION OF PATIENT
TYPE	DATE	RESULTS	
LAST NEGATIVE			POSITIVE REACTOR *(No previous test or unknown)*
			INTIMATE CONTACT WITH ACTIVE TB CASE
SCREENING *(State type)*			CASUAL CONTACT WITH ACTIVE TB CASE
			CONVERTER
INTERMEDIATE PPD			OTHER *(Explain)*

MEDICAL HISTORY

	DATE	RESULTS
CHEST FILMS		

RECOMMENDED FOR INH CHEMOPROPHYLAXIS

YES	DATE STARTED	NO	REASON

CASE CLOSURE INFORMATION — DATE OF CLOSURE

REASON *(Check applicable block)*

- COMPLETION OF ADEQUATE THERAPY
- SUPERVISION NO LONGER NEEDED
- DATE INH COMPLETED
- ALLERGIC REACTION
- REFUSED SUPERVISION
- ELEVATED SGOT's
- OTHER *(Explain in Remarks)*

REMARKS:

BASELINE AST_____ DATE_____

MONTHLY AST RESULTS

DATE	RESULT	DATE	RESULT	DATE	RESULT

TYPED NAME OF CLOSING PHYSICIAN	SIGNATURE

AF FORM 2453 PREVIOUS EDITION IS OBSOLETE

Computer Generated 62 MDG/SGOAM