

## **Preliminary relation of Commission of Italian Ministry of Defense on incidence of malignancy among Italian military personnel in Bosnia and Kosovo.**

The Commission of inquiry established by the Defense Ministerial Decree of 22 December 2000, chaired by Prof. Franco MANDELLI and composed by Prof. Carissimo BIAGINI, Prof. Martino GRANDOLFO, Dr. Alfonso MELE, by Dr. Giuseppe ONUFRIO, Dr Vittorio SABBATINI and Jan. Isp. Med. Antonio TRICARICO presents the first report on the work. The task of the Commission was to ensure all medical and scientific aspects of the cases emerged and came to the attention in recent times cancer in military personnel, particularly in the military who have played operations in Bosnia and Kosovo, and see whether there is correlation with depleted uranium munitions used in that area, or if they are identifiable causes at the root of these various diseases. In this first report shows the incidence of cases of malignancies with a confirmed diagnosis compared with the data of the Italian Cancer Registries (Appendix 1). As regards the role of depleted uranium are exposed some preliminary considerations arising from the data available in literature and the results of campaigns measurements taken from Italian and international organizations. The role of other causes was not addressed as required, if deemed appropriate, a further study. It is strongly advised that close monitoring over time, both as regards any new cases, both for checks to be carried out on other populations at risk. The time taken for the preparation of this report is derived from the need to collect all the data concerning the military who have played operations in Bosnia and Kosovo and verify the diagnosis of malignant neoplasms.

### **EPIDEMIOLOGICAL ASPECTS**

#### **POPULATION, DATA SOURCES AND METHODS**

The population which has been calculated the incidence of cancer is formed by the military since December 1995 to January 2001 have made at least one mission in Bosnia and / or Kosovo. The list of such persons has been provided by Member More of the Army, Air Force, Navy and Police, the Directorate General of Military Health who transmitted it to the Superior Institute of Health. For each subject are currently available the following information: date and place of birth, residence, and capable armed force, belonging department, location of placement department, where localities have conducted missions, start date and end of them.

The cases that come partly from spontaneous reports were communicated by Defence. For each action taken in using diagnostic confirmation certificates and copies of medical records provided by departments of diagnosis and treatment, university or hospital, oncology and hematology.

Have not been taken into consideration cases without documented diagnosis and those diagnosed with non-neoplastic diseases. The cases reported, the documentation had not gained sufficient for the definition of the diagnosis, were not currently taken into account.

The calculation of incidence rates has been done recitals in the numerator the number of cases for each disease reported in the denominator amount of time of observation for each subject (from the date of the first mission to 31 days in January 2001, the date on which they were Acquired data from the Istituto Superiore di Sanita, or the date of diagnosis for cases). They were calculated rates for specific age five classes for the following diseases: Hodgkin's lymphoma (LH), Non-Hodgkin's lymphoma (LNH), Linfatica Acute leukemia (ALL), total disease emolinfoproliferative observed, total solid tumours and total malignant tumours recorded. For each rate has been estimated ranges of the 95% confidence interval (95% CI) applies to the range of values within which may sway the estimates of incidence rates as a result of the case.

Comparison of the incidence rates of the population studied was done with those of the male population covered by the cancer registries Italians. Evidence cancer incidence data collected on the basis of diagnosis confirmed. Used were 9 registers which data were available updates (see Appendix 1). The data used refer to the period 1993-1997. As indicator for the comparison has been

used in the ratio of cases of cancer "observed" people in the military who went to Bosnia and / or Kosovo and "expected" in the same population, referring to the rates of cancer registries Italian: the relationship between cases "observed" in cases "expected" gives a measure of risk called SIR (Standardized Incidence Ratio). When there is no difference between observed and expected cases this ratio is equal to 1, while a value greater means a number of observed cases higher than expected and vice versa for a lower one. Even for SIR were calculated confidence intervals. To make the study population more homogeneous and easy to make comparisons with data from the Registries tumors operating in Italy, the analysis was restricted to age groups between 20 and 49 years which include the 97.1% of the group of Italian soldiers went on a mission in Bosnia and / or Kosovo (not occurred in the age groups excluded). Since age groups excluded are low, the number of cases expected in those bands is zero for zero is the number of observed cases, as a result of the calculation SIR is not influenced in any way by the selection. The calculation of rates and the SIR was also taking into account the latency period between exposure and disease observed. Because literature is not included data about the latencies, has been suggested a minimum latency of 12 months. They were not be all those persons who had an observation period of less than 12 months (from both the numerator - either from the denominator) and, for each subject were removed first 12 months of observation (at that time not were at risk of developing the disease because of exposure in the studio).

## RESULTS

The Tables 1 and 2 describe the population studied by age and region of birth. Overall, we analyzed 39,450 soldiers, including 38,343 in the 20-49 age groups, the total observation time was 81,460 person-years. Most of the population (84.5%) came by.

Table 1. Distribution of the study population, current age and the Armed Forces.

Table 2. Distribution of the study population for the Armed Forces and geographic area of birth.

Table 3. Distribution of the study population, the Armed Forces and 1 ° year mission.

In Tables 4 and 5 are the distribution of subjects location of use and number of missions. The 68% of the subjects completed a single mission, the two missions 23.5% and 8, 7% more than two.

Table 4. Resort destination missions for the Armed Forces.

Table 5. Distribution of the subjects for the Armed Forces and number of missions.

Table 6 presents a description of the cases. 4 have been reported LNH, 9 LH, LLA 2 and 13 solid tumors. Twenty cases belong to, 2 and 3 Military all'Aeronautica the Carabinieri.

Table 6. Description of the cases 31/01/2001.

Table 7 shows the specific incidence rates by age and disease.

Table 7. Incidence rate (per 100,000 person-years) and confidence intervals at 95% of diseases detected, by age group.

Table 8 shows, by the calculation of SIR, the comparison with the data of Cancer Registries.

Table 8. SIR by type of pathology.

Table 9 shows the values of SIR, calculated assuming a minimum latency period of 12 months for

various diseases, were therefore excluded cases occurred before 12 months after exposure.

Table 9. SIR by type of pathology, assuming a latency period of 12 months.

Table 10 are compared day stay in Bosnia and Kosovo or the subjects who had a diagnosis of malignant disease, compared to those who have not developed diseases.

Table 10. Days spent in Bosnia and Kosovo or in the cases and not in cases.

## EXPOSURE TO RADIATION AND LINFOMA OF HODGKIN

From a radiological point of view, depleted uranium, as all elements emit radiation weakly penetrant which, in particular, the alpha radiation, will weigh health in the case of internal exposure through inhalation, ingestion or l' incorporation through wounds. Regarding the possible causal link between Hodgkin's disease and internal exposure, in the current state of knowledge, you can retrieve the following information. The recent extensive review of the Report UNSCEAR 2000 (United Nations Scientific Committee on the Effects of Atomic Radiation) (1), which due to its undisputed authority is a clear reference to international level, reports, in the chapter on the Hodgkin's lymphoma, three studies for the exhibit dall'isotopo iodine I131, radioisotope which does not emit alpha radiation, as opposed uranium: the two studies do not show any significant causal relationship (2,3,4). Two works (5,6), are relative to patients treated with the thorotrast, a solution used as a contrast to the '50s and are based on a few cases (1 case in Danish and 2 in the German) and the third concerns the work that exposure to radon gas (Rn222) not mine analyzes the number of cases occurred in connection with exposure levels (7).

Two other similar cases are carried over from previous UNSCEAR Report of 1994 and affect workers involved in mineral processing uraniumiferous, which are professionally exposed to dust containing isotopes of uranium and thorium (8,9). In a context in which the incidence of lung cancer and bone was lower than expectation, there has been in 20 years of the observation period, some cases in excess of other diseases, including 3 cases of lymphoma Hodgkin. Recently, important lessons have emerged from epidemiological studies of two cohorts of workers in production plants and nuclear fuel ponovno (10,11). In these studies was analyzed the correlation between external exposure (ie not through inhalation, ingestion or incorporation) cumulative mortality and cancer. In particular, in the first, was considered the correlation between external exposure and morbidity. In both studies found is a statistically significant association between Hodgkin's lymphomas of external exposure and, when used a delay of 10 years between exposure and onset of illness, but it concludes that there may be a causal relationship, because that would be contrary to the findings of the tests on survivors of Hiroshima and Nagasaki and other studies (1, 12, 13). As is pointed out by other authors (14), these studies do not consider, however, the role of internal and other risk factors (eg. Smoking). It 'obvious that the reconstruction of internal exposure data and other confounding is extremely complex, since the use of historical records of cancer. However, Mc Geoghean and Binks (10) expect to embark on a retesting data on the basis of information obtained on exhibit. These future results may perhaps contribute to better clarify the role of internal contamination of uranium in the etiology of lymphomas. Several other studies have finally analyzed cases groups (clusters) of the onset of lymphoma Hodgkin's, but have not found an explanation unique, so much so that it was also suggested association with viral forms.

Defined the state of knowledge emerged from epidemiological studies, it is considered useful to recall some considerations closely radioprotezionistico profile. From estimates of risk based on the survivors of Hiroshima and Nagasaki, which still form the basis of epidemiological data on which the fundamental processes radiation risk estimates (12), does not show a significant correlation between exposure and incidence of lymphomas, especially for Hodgkin's, and also for non-Hodgkin

(15). However, note that these estimates are taken from an exhibition external uniform, and predominantly acute radiation range. The exposure scenario that prefigures, in the case of the Italian contingent in Kosovo and Bosnia, it is profoundly different. Indeed it can be assumed that, given the prevailing emissions of depleted uranium (alpha and beta), in this case exposure is modest external entities, the main mode of exposure must be considered internal, alpha and beta radiation, probably chronic and predominantly inhalation and / or in part if swallowed. And 'then reasonable doubt that the risk factors developed from the data of survivors of Hiroshima and Nagasaki could adequately represent an even exposure scenario so different as that of the Italian contingent.

You should also consider that, particularly in the case of inhalation of insoluble uranium oxide, it is expected that the target organs, and then subject to a higher exposure are the lungs, where it is estimated (16) that a not insignificant fraction of 'assets deposited in these concentrates in mediastinal lymph nodes. In light of the above, a causal relationship between Hodgkin's disease and internal exposure, in the current state of knowledge, has never been demonstrated. The studies cited, also referring to chronic exposure for a long time in conditions of exposure other than those considered by the military here. While taking into account as stated above, the excess cases of Hodgkin's lymphomas, although at the time not statistically significant, deserves to be studied carefully, so it is considered necessary to follow the temporal evolution of any database .

## POSSIBLE EXPOSURE OF ITALIAN MILITARY TO DEPLETED URANIUM

With regard to exposure of soldiers in the Balkans, we should remember that the estimates available in the Report of the ANPA 2000 (17), with extensive journal of literature of American military source, indicate, as critical scenario ( "worst case") for ' inhalation of uranium dust, the one on the impact of a surface on penetratore armoured media, reaching an estimated effective dose of 22.6 mSv. This dose is considered an upper limit and is reported to persons present in the immediate vicinity of the dart struck at the moment of impact.

The recent report of the mission UNEP (United Nations Environmental Program) in Kosovo (18) that carried out the mission last November in 11 sites with a team of experts from various countries, including, for Italy, a technician of ' ANPA, provides useful guidance. The report concludes that there was not a significant contamination of the areas subject to mitragliamento with darts to depleted uranium, except at the point of contamination were found where the darts. They do not, however, a significant risk of contamination of air, water or plants. It was not detected any contamination of water, milk, buildings or objects.

The UNEP estimates that the possible ingestion of dust taken inadvertently touching a point of contamination "has no significant radiological hazards, but in this case the chemical risk is somewhat 'higher health standards apply. The results of the campaign UNEP measures are in substantial agreement with those of the measurements taken by CISAM (Interforze Studies Center and Military Applications). The assessment of exposure to depleted uranium in Italian soldiers will be carried out through analysis, still in Corsican, which still require a few months time. This is in view of the need to have a significant group of soldiers to the first experience whose urine be analysed before and after the mission. Moreover, the period of exposure winter is the least significant from the point of view of resuspenzijo dust for the specific climatic conditions. It should be pointed out, however, that screening for a group of German soldiers, which prompted a period of a year and a half, did not reveal exposure to depleted uranium (19). For completeness of analysis, the sample of soldiers also will be subjected to analysis "Whole Body Counter" at high and low energy. From the information currently available, there are elements that can make believe that there has been a significant exposure to uranium compounds. The findings of the analysis will still better assessment of the situation.

## PRELIMINARY CONCLUSIONS

1) For malignancies (haematological or not) emerge together a number of cases lower than expected. This result may be due in part to physical fitness for selection to which they have carried out military and partly to the fact that the expected were calculated on the basis of Cancer Registries coming mainly from the north where the incidence of cancer overall is higher compared to the South (from which came the most soldiers deployed in Bosnia and / or Kosovo).

2) There is an excess, not statistically significant, of cases of Hodgkin's lymphoma and leukemia Linfatica acute, but at present numbers that result may be due to chance especially for the LLA. Regarding LH LLA and it must be said that no such obvious geographical differences to overstate the expected. It is considered necessary to confirm the results obtained so far, and therefore it is suggested:

A. By updating the number of cases of cancer through the acquisition of the necessary documents to confirm reports diagnostics arriving in the coming months with a new report by the end of May.

B. As a follow over time a cohort of persons engaged in Bosnia and / or Kosovo. To this end should be assessed the feasibility of conducting a study that points to monitor the incidence of cancer.

C. By proposing to the other NATO countries that were committed in Bosnia and / or Kosovo, also in relation to studies already undertaken to identify uniform methodologies for evaluating the incidence of cancer in the military in their respective countries. This is to a confrontation and an overall assessment of the various studies.