

CYTOGENETIC AND RESPIRATORY CHANGES IN IONIZING
RADIATION OCCUPATIONAL EXPOSURE

Irina Anca Popescu, Doina Havarneanu, Iulia Roman, Doina Popa, Irina Alexandrescu
Institute of Public Health Iasi, Romania

Abstract:

Aim. The study was aimed to investigate the respiratory/cytological and cytogenetic changes in subjects at risk of occupational ionizing radiation by new national recommendations and other sensitive methods.

Material and methods. There were investigated 30 subjects, 18 females – 60%, from diagnostic nuclear medicine/radiotherapy and radiochemistry laboratory with a mean exposure length of 14.2 ± 6.8 years to gamma radiation. They were investigated by: physical, E.N.T and pulmonary function exams, as hematological tests for blood cells' count and morphology, cytological exams in both sputum and oral exfoliated cells. Cytogenetic investigation consisting in micronuclei (MN) test in peripheral lymphocytes culture cells was performed in all subjects as well as individual dosimetry.

Results. There were diagnosed allergic rhinitis (20%) and contact dermatitis (11.1%) at radiopharmaceuticals preparation and use, without any impairment of lung function. In 8.3% Co-therapy subjects there were diagnosed chronic rhinitis, correlated with under 10 years of gamma-rays exposure ($p < 0.05$). Hematological effects were of lymphopenia positively correlated with very long-term radiation exposure. In 6.6% cases were revealed numerical disorders of MN in peripheral lymphocytes and 16.6% subjects had associated structural lymphocytes damages significant correlated with a high exposure level ($p < 0.001$). Incidence of high MN number in oral exfoliated cells correlated both in blood in 3.3 % subjects. Sputum cytology was of type I and II in 80%, respectively 16.6% cases with 1 case of MN presence. Individual dosimetry showed admitted legal values.

Conclusions. Staff involved in the use of ionizing radiation, recently monitored in Romania, seem to have an unquestionable respiratory carcinogenic risk, even at low ionizing radiation doses. MN test in oral mucous exfoliated cells, concomitant in peripheral lymphocytes cultures is of much specificity in occupational ionizing radiation assay and correlates in our study with the exposure levels.

Key words: ionizing radiation, gamma emitters, occupational exposure, respiratory/ cytological and effects, cytogenetic exam

Cytogenetic And Respiratory Changes

Rezumat:

Scop. Scopul studiului a fost de a evalua modificările clinice și citologice/respiratorii precum și cele citogenetice la persoanele expuse profesional la radiații ionizante, utilizând recomandările din fișa de noxe din normele generale de protecția muncii dar și noi metode cu specificitate pentru acest tip de expunere. Material și metode. S-au investigat 30 de subiecți, 18 femei (60%), provenind din sectorul medical (radioterapie și medicină nucleară) și învățământ universitar (cercetare radiochimică) având o medie a expunerii ocupaționale la radiații ionizante gama de $14,2 \pm 6.8$ ani. Investigațiile efectuate lotului au constat în: examen clinic general, examen O.R.L., probe functionale respiratorii, teste hematologice complete și examen citogenetic (testul micronucleilor - MN- în culturi de limfocite periferice). Pentru subiecții implicați în prepararea radiofarmaceuticelor bazate pe radionuclizii gama emițători (generator de ^{99m}Tc și ^{131}I) s-au efectuat investigații citologice în probe de spută și în celulele exfoliate recoltate de la nivelul mucoasei orale. Monitorizarea expunerii s-a bazat pe dozimetria individuală.

Rezultate. Au fost diagnosticați 20% subiecți cu rinită alergică și 11,1% cu dermite de contact apărute ca urmare a activităților de preparare și utilizare a radiofarmaceuticelor, fara obiectivarea unei alterări a funcției pulmonare. La 8,3% din subiecții din cobaltoterapie s-au diagnosticat rinite cronice corelate cu expuneri ocupaționale de până în 10 ani ($p < 0,05$). Hematologic s-a evidențiat o limfopenie statistic semnificativă pentru subiecții cu o foarte îndelungată expunere profesională. Modificările citogenetice de tip numeric au apărut la 6,6% din subiecți iar cele de tip structural la 16,6% din cazuri, fiind statistic semnificative ($p < 0,001$) și corelate cu un nivel acut recent de expunere la radiații ionizante. Incidența numerică crescută a MN în limfocitele periferice s-a corelat cu cea din celulele exfoliate bucale pentru 3,3% din subiecți. Citologia sputei a fost de tip I și II la 80% și respectiv 16.6% din cazuri și într-un singur caz s-au obiectivat MN. Dozimetria individuală a evidențiat valori ale expunerii profesionale la radiații ionizante încadrabile în limitele legal admise.

Concluzii. Persoanele expuse profesional la radiații ionizante, monitorizate recent din punct de vedere al stării de sănătate, prezinta un risc carcinogen la nivelul aparatului respirator, chiar și la doze mici de expunere. Testul citogenetic al MN în culturile de limfocite periferice efectuat concomitent cu citologia în celulele exfoliate orale demonstreaza o mai mare specificitate pentru corelarea cu nivele de expunere la radiații ionizante.

Cuvinte cheie: radiații ionizante, emițători gama, expunere profesională, efecte respiratorii/ citologice, test citogenetic

INTRODUCTION

Gamma rays are electromagnetic radiations similar with x-rays, light and radiowaves. The greatest part of the annual average dose of radiation comes from natural environmental

.....Sfârșit de coloană.....

it de secți sources. Every person is exposed to an average of 2.4 mSv/year radiation from natural sources. (1).

Gamma radiation is an ionizing radiation which can cross the biological tissue, having no mass,

.....Sfârșit de secțiune (Continuu).....

no burden. By passing through the cells it determines the occurrence of some ionizing processes, a stimulation of the electrons belonging to the structures of the atoms that are constituents of the biological molecules. (2,3). Each track of low linear energy transfer (low-LET), such as gamma rays, consists of only relatively small number of ionizations across cell nucleus, but with direct and indirect effects to DNA damage. (2). The exposure to ionizing radiation damages DNA and causes mutation and chromosomal changes in cells and organism. Damage by radiation also leads to cell transformation (a stage in cancer development) and cell death. In dividing cells, ionizing radiation causes mitotic abnormalities such as aneuploidy, micronuclei (MN), and multinucleated cells by direct interference with segregating chromosomes. The scoring of chromosome aberrations in human peripheral blood lymphocytes provides a sensitive method for biological dosimetry and also provides an approach to assess dose-response relationships for cytogenetic damages (2). The MN are unstable aberrations but they are considered, however, more sensitive for the detection of effects at low doses than are stable aberrations (2). The lymphocytes answer rapidly to low doses of ionizing radiation in the peripheral

Sfârșit de coloană

sectiune radiosensitive lymphocytes of human blood.

The lowest acute dose at which significant increases appear in lung adenocarcinoma have been observed in mice, for a dose of 2.5 Gy of gamma rays irradiation (Coggle) (2).

There is dependence between the sensibility of the tissues to the carcinogenic action of the ionizing radiation depending on the age and exposure doses. A possible confounding factor is the quantification of the carcinogenic risk due to low levels of ionizing radiation in occupational exposure. (2,4). At low doses of low-LET radiation there is a linear relationship between dose and the frequency of genetic effects studied (4).

In nuclear medicine radiopharmaceuticals are administered diagnostically to patients to study tissue morphology and organ function. Romania is considered as a country with health care level I in utilizing nuclear medicine with an average of 19 diagnostic nuclear medicine procedure per 1,000 population, as reported in 2000 (1). The distribution of global annual collective effective dose according to health care levels is giving for countries level I a mean dose of 0.008 mSv per caput and 1.3 (1.1) mSv per person per year. Practices with radiopharmaceuticals remain small comparing with X-rays uses, the mean dose per procedure is larger for nuclear medicine (4.6

Sfârșit de secțiune (Continuu)

Cytogenetic And Respiratory Changes

mSv) than for medical x ray (1.2 mSv) (1).

Our study was aimed to assess both cytogenetic and respiratory damages in subjects with occupational exposure to ionizing radiation by new national recommendations and other sensitive methods (5)

The paper presents aspects concerning cytogenetic and cytological respiratory changes due to ionizing radiation, well known as certain human carcinogenic agent.

MATERIAL AND METHODS:

Sfârșit de coloană

We investigated 30 subjects, working in health care system (nuclear medicine, radiotherapy) and radio-chemistry research laboratory, all of them with occupational exposure to gamma radiation (^{99m}Tc generators, radionuclides based on ¹³¹I in nuclear medicine, ⁶⁰Co, in radiotherapy or irradiators using different sealed sources for research purposes).

The structure of the studied group:

- distribution by sex categories: 18 F (60%), 12 M (40%) (Fig. 1)

Sfârșit de secțiune (Continuu)

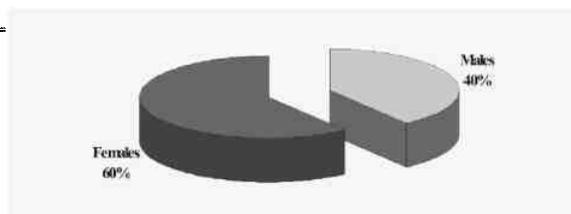


Fig. 1 Distribution by sex categories

- mean age: 42.4±12.57 yrs old

Sfârșit de coloană

mean exposure length to gamma radiation: 14.2±6.8 years (Fig. 2)

Sfârșit de secțiune (Continuu)

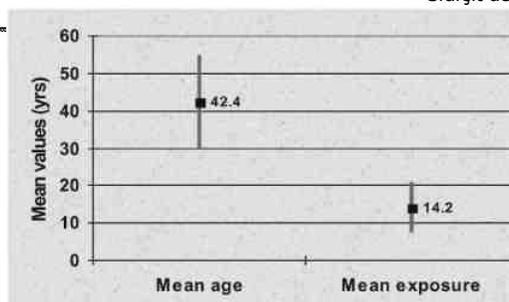


Fig. 2 Mean age and exposure length

distribution by profession: 26.6% chemists, 3.3% chemical operator - doctors, 60% nurses, 10% (Fig. 3)

Sfârșit de coloană

Sfârșit de secțiune (Continuu)

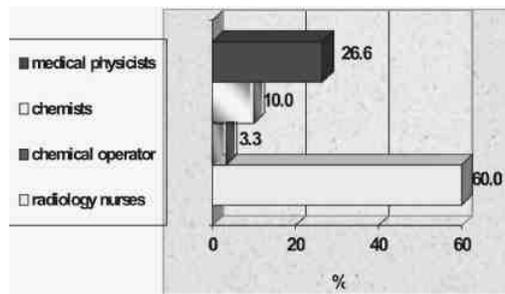


Fig. 3 Distribution by profession

- distribution by smoking habit: 10%
- Protocol investigations consist of:
- monitoring of the exposure by individual dosimetry
 - occupational anamnesis
 - physical exam
 - ENT specialty exam
 - Pulmonary function test
 - hematological exam (complete blood count - Hb, Hct, RBCs, RBC indices, WBC, platelet, reticulocytes, lymphocytes and blood cells` morphology)
 - cytogenetic investigation – micronuclei (MN) in culture of peripheral lymphocytes (number of cells with MN/ 1000 counted cells) -simple, nonexpensive screening technique - Moorhead method
 - cytological investigation in sputum (Babes - Papanicolau classification) and in oral epithelial exfoliated cells – by oral mucous brushing (for the first time performed in Romania, at Iasi) - non-invasive, cheap and

----- practical methods

RESULTS AND DISSCUSION:

Radiopharmaceuticals emit penetrating gamma-radiation and give rise to the exposure of nuclear medicine staff and other persons in the vicinity of patients undergoing diagnostic or treatment.

The annual effective dose to monitored workers worldwide, averaged over five-years period, was with a mean value of 1.0 mSv in nuclear medicine, with an average of 1.3 mSv at exposed workers from radiotherapy and of 1.1 mSv at exposed staff from educational establishment. (1).

At all investigated subjects the individual dosimetry monitoring showed admitted limits (170µSv/month). Clinical and specialty exams diagnosed, as chronic respiratory effects, 20% allergic rhinitis and 11.1% contact dermatitis (with history of specific symptoms) at subjects from

-----Sfârşit de secţiune (Continuu)-----

Cytogenetic And Respiratory Changes

radiopharmaceuticals preparation and use, but without any bronchospastic symptoms or respiratory obstructive impairment. Also, no other nonspecific bronchial hyperresponsiveness were

Sfârșit de coloană

observed. At 8.3% subjects from Co-therapy we found chronic rhinitis correlated with 1 to 10 years of gamma-rays exposure ($p < 0.05$). (Fig.4).

Sfârșit de secțiune (Continuu)

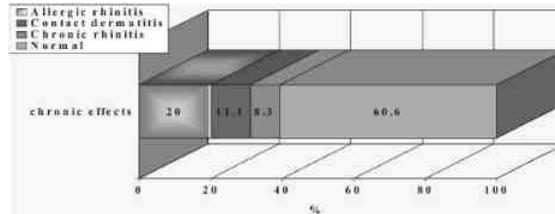


Fig. 4 Chronic effects (respiratory and dermatological)

Work involving the preparation and assay of radiopharmaceuticals tend to be associated with the length of occupational exposure in this field,

Sfârșit de coloană

thus hematological effects were of lymphopenia (blood lymphocytes level below 25%) positively correlated with over 30 years long term radiation exposure. (Fig. 4 bis).

Sfârșit de secțiune (Continuu)

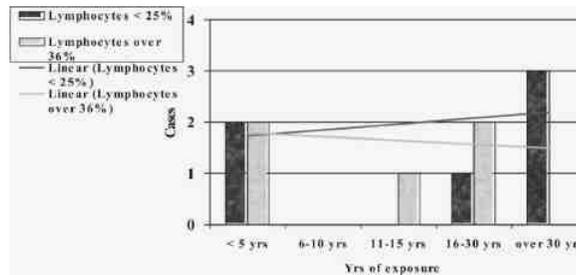


Fig. 4 bis Hematological chronic effects

Cytogenetic investigation revealed an incidence of 16.6% numerical (over admitted limit of

Sfârșit de coloană

4% MN) and structural (binucleus, atypical nucleus) (Fig. 5)

Sfârșit de secțiune (Continuu)

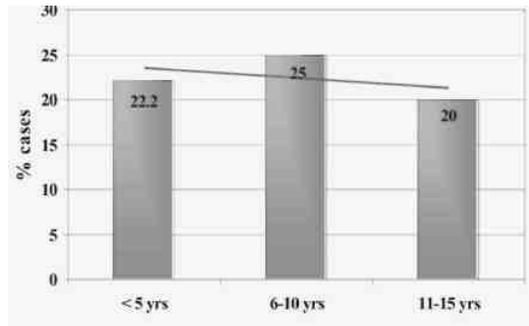


Fig. 5 Distribution of MN over normal range in blood peripheral lymphocytes by length of ionizing radiations exposure

disorders of MN in gamma-ray exposure, in non-smokers, under 40 years old and mainly men cases (25%). (Fig. 6).
Sfârșit de coloană

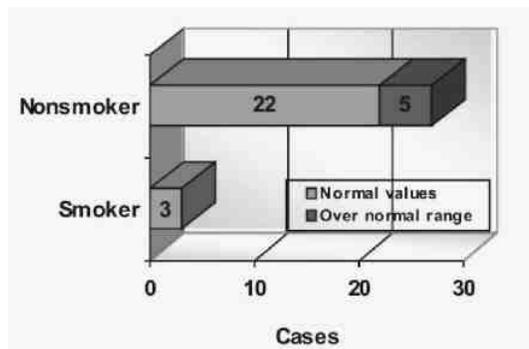


Fig.6 Distribution of MN over normal range in blood peripheral lymphocytes by smoking habit

80% of this damage correlated with less than 10 years of occupational exposure. We presume that the high incidence of numerical lymphocytes changes at persons with less than 10 years of occupational exposure is a biological response resulting from the noxious aggression. The increasing length of ionizing

Sfârșit de coloană

radiation exposure seems to develop an adaptive hematological response consisting in a decreased MN level in the peripheral lymphocytes. Table 1 shows the distribution of the frequency rates of MN in Gamma-ray exposure, by length of occupational exposure, sex and age distribution and smoking habit.

Sfârșit de secțiune (Continuu)

Cytogenetic And Respiratory Changes

DISTRIBUTION OF MN IN PERIPHERAL LIMPHOCYTES				
FREQUENCY (%) of MN in peripheral lymphocytes	Distribution of cases (% in total group)	Distribution of cases by sex categories (% in total group)	Distribution of cases by smoker / nonsmoker (% in total group)	Distribution of cases by age: <40yrs=40yrs (% in total group)
0-4	25 (83.3%)	9M(75%) / 16F(88.9%)	3 (12%) / 22 (88%)	16(64%) / 9 (36%)
5-10	3 (10%)	2M(16.6%) / 1F(5.5%)	0 / 3 (11.1%)	2 (66.6%) / 1 (33.3%)
>15 MN and lymphocytes damages	2 (6.66%)	1M(8.3%) / 1F (5.5%)	0 / 2 (7.4%)	1/1
>4 MN and lymphocytes damages	5 (16.6%)	3M(25.0%) / 2F (11.1%)	0%/18.5%	3 (60%) / 2 (40%)

DISTRIBUTION OF MN BY LENGTH OF IONIZING RADIATIONS EXPOSURE				
FREQUENCY (%) of MN in peripheral lymphocytes	Distribution (% in total group) < 5 yrs exposure	Distribution (% in total group) 6-10 yrs exposure	Distribution (% in total group) 11-15 yrs exposure	Distribution (% in total group) >15 yrs exposure
0-4	8 (32%)	6 (24%)	4 (16%)	7 (28%)
5-10	1 (3.33%)	2 (6.66%)	-	-
>15 MN and lymphocytes damages	1	-	1	-
>4 MN and lymphocytes damages	2 (22.2%)	2 (25%)	1 (20%)	-

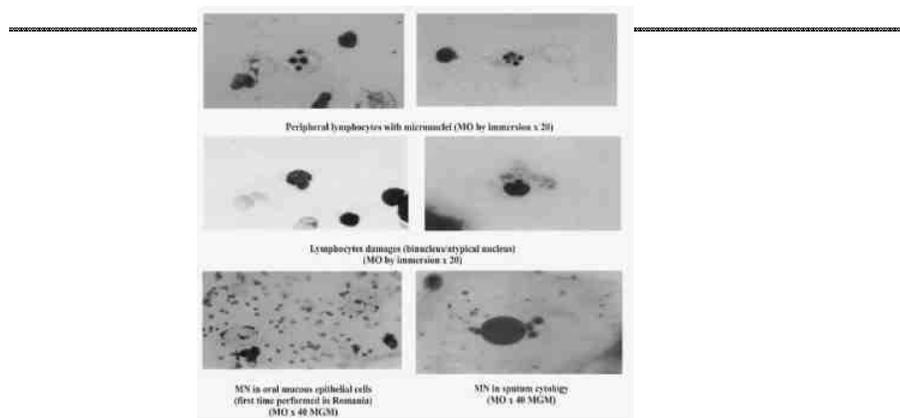
Table 1 Distribution of MN

Associated 8.3% frequency of lymphocytes damages correlated $p < 0.001$. We observed that in all this lymphocytes abnormalities cases the subjects described a recent history of high exposure event (exposure to ionizing radiation as their own diagnostic radiology).

Cytological exam in oral exfoliated cells, performed for the first time in Romania, showed 1 case of MN at a nonsmoker male subject having less than 40 years old which was in direct correlation with peripheral lymphocytes MN numerical disorders (Fig.7).

Sfârșit de coloană

Sfârșit de secțiune (Continuu)



7 MN in peripheral lymphocytes and respiratory cells

It seems that the length of ionizing radiation occupational work per day of this subject in environment exceeded a legal

Sfârșit de secțiune (Continuu)

Fig.

admitted exposure (6 hours) in the few days preceding the cytogenetic and cytologic tests.

Table 2 presents the results of cytological exam by the four existing types of Babes-Papanicolau classification and also by age, sex distribution, length of occupational

ionizing radiation exposure and smoking habit. Sputum cytology was of type I (normal) in 80% of cases, of type II (inflammatory) in 16.6% of cases and 1 case of sputum MN presence, having no smoking habit correlation.

Sfârșit de secțiune (Continuu)

DISTRUBUTION OF FREQUENCY RATES OF MN IN ORAL EPITHELIAL CELLS				
Frequency (% of MN in oral epithelial cells)	Distribution of cases (% in total group)	Distribution of cases by sex categories (% in total group)	Distribution of cases by smoker / nonsmoker (% in total group)	Distribution of cases by age: <40yrs/=40yrs (% in total group)
0-4	29 (96.6%)	11M(91.6%) / 18F(100%)	3 (10.3%) / 26 (89.6%)	17 (58.6%) / 12 (41.3%)
>5	1 (3.3%)	1 M (8.3%)	0 / 1 (3.3%)	1 (5.5%) / -

DISTRUBUTION OF FREQUENCY RATES OF MN IN SPUTUM				
Sputum cytology	Distribution of cases (% in total group)	Distribution of cases by sex categories (% in total group)	Distribution of cases by smoker / nonsmoker (% in total group)	Distribution of cases by age: <40yrs/=40yrs (% in total group)
Cytology type I (normal)	24 (80%)	9M(75%)/15F(83.3%)	3(12.5%)/0	17(70.8%)/7(29.2%)
Cytology type II (inflammatory)	5 (16.6%)	2M(16.6%)/3F(16.6%)	-	1(20%) / 4 (80%)
MN in sputum	1 (3.3%)	1 M (8.3%)	-	-

Table 2 MN in respiratory cells

CONCLUSIONS

- Staff with occupational ionizing radiation exposure in Romania are monitored by new national recommendation for three years.
- Persons with ionizing radiation occupational exposure seem to have an unquestionable respiratory carcinogenic risk, even at low ionizing radiation doses.
- Micronuclei test in oral mucous exfoliated cells, at first time performed in Romania, concomitant in peripheral lymphocytes cultures is of much

Sfârșit de coloană

specificity in occupational ionizing radiation assay and correlates, in our study, with the exposure level.

- As a new exam in our legislation, the MN test although unspecific, can bring useful information on occupational personnel' exposure and, it had no correlation with smoking habit or length of occupational exposure.
- We presume that MN high levels and lymphocytes damages vs clinical diagnosis are early malignant signs due to cancer

Sfârșit de secțiune (Continuu)

Cytogenetic And Respiratory Changes

first noted as a high cytogenetic frequency effect. • Individual monitoring programmes for health status and assessment of personal dose equivalent emphasize a real recording of staff with occupational ionizing radiation exposure.

ACKNOWLEDGEMENTS:

The paper was presented at the European Respiratory Society (ERS) Annual Congress held in Copenhagen, Denmark from September 17 - 21, 2005, due to Silver Sponsorship offered by the ERS.

REFERENCES:

1. xxx - International Basic Safety Standards (BSS) for Protection Against Ionizing Radiation and for the Safety of Radiation Sources. 115, Safety Standards. IAEA, 1996
2. xxx - United Nations Scientific

Committee on the Effects of Atomic Radiation (UNSCEAR) 2000 Report, vol II annex G: Biological effects at low radiation doses, vol I, annex E: Occupational radiation exposure

3. xxx - "1990 Recommendations of the International Commission on Radiological Protection", Pergamon Press, Oxford: 1991 (ICRP 60)
4. xxx - International Agency for Research on Cancer Study Group on Cancer Risk among Nuclear Industry Workers. Direct estimates of cancer mortality due to low doses of ionising radiation: An international study, Lancet 344, 1039-1043, 1994
5. xxx - National Occupational Safety Regulations (NGPM), 2002

.....Sfârșit de coloană.....

.....Sfârșit de secțiune (Continuu).....