

COMBINED EFFECTS OF SIMULTANEOUS γ -RAYS IRRADIATION AND INHALATION OF BENZENE, TOLUENE AND CARBON MONOXIDE ON RABBITS

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Abstract Combined effects on rabbits induced by γ -rays irradiation in combination with inhalation of benzene, toluene and carbon monoxide and the interactive characteristics (antagonistic, additive or synergistic) of these agents were studied. Ninety healthy male rabbits were equally divided into 9 groups, eight of which were test groups assigned according to four-factor- two-dose-level orthogonal layout [$L_8(2^7)$] program and one was the control. The two dose-levels of the four factors were: for γ -rays irradiation, 0.0075Gy/d and 0.0375Gy/d, and for benzene, toluene and carbon monoxide, $40 \pm 15 \text{mg/m}^3$ and $182 \pm 33 \text{mg/m}^3$, $90 \pm 30 \text{mg/m}^3$ and $407 \pm 68 \text{mg/m}^3$, $93 \pm 4 \text{mg/m}^3$ and $278 \pm 8 \text{mg/m}^3$ respectively. The animals were exposed to γ -rays irradiation combined with benzene, toluene and CO vapor 2h a day and 5days a week for a period of 8 weeks. Experimental results were analysed with the method of variance analysis and the test groups were compared. The results showed that (1) the interactive factor, the ratio (ω) of the combined effects caused by the four agents to the sum of the four independent effects induced by those agents, was 2.16, 1.58, 2.07, 2.67, 1.31 and 1.18 for dicentric + ring, acentric, aberration cells, total aberration, micronuclei and SCEs/C in lymphocytes respectively, and the ratio for aberrant sperms was as high as 5.97. The ratios showed that interactions were mainly synergistic ($\omega > 1$). However, for acentric interactions between γ -rays and benzene was antagonistic. (2) The four agents could all obviously cause decrease in testis weight index, and γ -rays, benzene and CO could markedly reduce the number of sperms and increase the ratio of aberrant sperms. The interactions between γ -rays and benzene for the decrease in testis weight index and for the elevation of the ratio of aberrant sperms were synergistic. (3) CO could cause decrease in total amount of leucocytes, thrombocytes and hemoglobin, and toluene cause decrease in lymphocytes. (4) Gamma rays irradiation combined with inhalation of benzene, toluene and CO could produce significant interactions which were mainly synergistic, and CO, when combined with γ -rays, benzene and toluene, could cause obvious effects on gland.

KEYWORDS γ -rays, Benzene, Toluene, CO, Combined effect, Interactive factor

CLC Q345, Q691, Q504, R818.03

Research on the combined effects of ionizing radiation with other physical or chemical agents is an important field in radiation protection. An excellent review and in the field was published by UNSCEAR in its 1982 report.^[1] Previous studies concerning combined effects mostly deal with two agents. In some circumstances, however, the number of agents involved is obviously far more than two. For example, γ -radiation, radon and its daughters, uranium ore dust, diesel engine exhaust fumes, and other substances exist in a uranium mine^[2], and in a nuclear-powered submarine, there exist noise pollution, and a great many trace gases, in addition to γ -radiation^[2,3]. The combined effects of γ -radiation and multiple agents are very complicated and difficult to study, particularly in the case of chronic and prolonged effects. In this study the combined effects of simultaneous

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γ -rays irradiation in combination with benzene, toluene and carbon monoxide inhalation were observed with emphasis on the analysis of the combined effects on rabbit hemocytes and sex gland.

1 Materials and methods

The experiments were conducted in a simulated chamber with an inside diameter of 3.17m and height of 2m. Gamma irradiation was carried out with a ^{60}Co γ point source, from which the distance to center of the chamber is 3.16m. Doses of whole-body γ irradiation for all animals at same dose level were the same and exposures of the 2 sides of animal body were identical. During the experiments the concentrations of three gases in air in the chamber were steadied with a special gas flow system.

1.1 Experimental animals and groups

Ninety healthy male rabbits with a weight of 3.20 ± 0.25 kg and age of 6~7 months were divided into 9 groups, eight of which were experimental groups designed in terms of four-factor-two-level orthogononal layout [$L_8(2^7)$] program and one was the control. There were 10 animals in each group. The animals were simultaneously exposed to γ -rays, benzene, toluene and CO vapor for 2h a day, and 5 days a week for a period 8 weeks.

1.2 Exposure levels of agents

Exposure levels to different agents were simply graded into two, i.e. the high and low levels, which were numerically represented by 1 and 2. The two dose-levels of these agents were: for γ -rays radiation 0.0375Gy/d ($\gamma 1$) and 0.0075Gy/d ($\gamma 2$), and for benzene(B), toluene(T) and CO. 182 ± 33 (B1) and $40 \pm 15 \text{mg/m}^3$ (B2), $407 \pm 68 \text{mg/m}^3$ (T1) and $90 \pm 29 \text{mg/m}^3$ (T2), $278 \pm 8 \text{mg/m}^3$ (CO1) and $93 \pm 4 \text{mg/m}^3$ (CO2), respectively. The cumulative dose of γ -rays irradiation was 1.5 Gy(1) and 0.3 Gy(2). The animals in the control group were not exposed to any agents.

1.3 Observed effects and methods

The observed effects in this study included chromosome aberrations, frequencies of sister chromatid exchanges (SCEs) and micronuclei of lymphocytes, and chromosome aberrations of bone marrow cells, ratio of aberrant sperms, testis weight index and number of sperms. The culture and preparation of lymphocytes were done according to the literatures.^[5,6] Chromosome analyses were carried out in metaphase of cells containing 44 centromeres. All detectable aberrations but the gaps were recorded. The observed chromosome aberrations included the dicentric plus ring (dicentric, centric ring and polycentric chromosome), the acentric (terminal deletions, minutes and acentric rings), aberration cells(chromosome type aberration cells), total aberrations and total aberration cells (chromosome type and chromatid type). The number of cells scored per rabbit was 200 for chromosome aberration and 30 for SCE. The Cyt-B method by Fenech M. *et al.*^[7] was used for measuring micronuclei. In the measurements of micronuclei in lymphocytes, 500 binuclear cells were observed in each sample of blood, and the diameter of micronuclei (appearing as round or ellipse, separating from its main nucleus or tangent with one) was less than one third of its main nucleus.

The testis weight index was the ratio of weight of both testes of the animal at the time when it was killed at the end of the experiment to the body weight before its slaughter. The number of sperms was counted with the method proposed by Wang Sheng, *et al.*^[8] The ratio of aberrant sperms was a percentage of that in 1000 sperms examined per animal. The method used for the

examination of aberrant sperms and other details could be found in published articles.^[9]

2 Results

Test results of combined effects are shown in Tab.1 to 4, and corresponding effects were different between the two dose levels, and the results of significance tests (F-test, variance test) by orthogonal design for different agents are listed in Tab.1a to 4a.

2.1 Chromosome aberration, micronuclei and SCEs in rabbit lymphocytes

Test results showed that (1) under the present experimental conditions the yields of chromosome aberration, micronuclei and SCEs/cell in lymphocytes for different test groups were all higher than that of the control. The significance test indicated that the differences in effects between the two levels were significant ($p < 0.01$); (2)when the dose level was raised, γ -irradiation could markedly increase the yield of chromosome aberration, micronuclei and SCEs/cell ($p < 0.01$). and the same results were found for benzene and toluene with acentrics as an exception. (3) Gamma radiation coupled with benzene could markedly indnce dicentrics+rings and micronuclei ($p < 0.01$), and the combined effect of γ -radiation and toluene could induce aberration cells ($p < 0.05$), and benzene in combination with toluene had significant effect on inducing acentric and aberration cells. However, no effect was seen for CO, which showed CO had no effect on lymphocytes.

Tab.1 Yields of chromosome aberration, micronuclei and SCEs in rabbit peripheral blood lymphocytes

Test groups	Dose levels				Chromosome aberration/%				Mn / ‰	Mnc / ‰	SCEs/C
	γ	B	T	CO	D + r	Ace	Abc	Tabc			
1	1	1	1	1	1.80	1.70	3.50	3.60	25.1	21.4	4.35
2	1	1	2	2	1.30	1.30	2.55	2.60	22.2	19.6	4.22
3	1	2	1	2	1.05	1.40	2.45	2.45	19.2	17.6	4.05
4	1	2	2	1	0.55	1.95	2.35	2.35	17.8	15.8	3.98
5	2	1	1	2	0.40	1.05	1.45	1.75	9.2	8.6	4.20
6	2	1	2	1	0.15	0.70	0.85	0.95	7.8	7.0	3.88
7	2	2	1	1	0.22	0.44	0.60	0.60	7.2	6.8	3.82
8	2	2	2	2	0.05	0.80	0.85	1.05	5.8	5.8	3.76
Control					0.00	0.30	0.30	0.40	3.0	3.0	3.59

Note: B=Benzene, T=Toluene; D+r=Dicentrics+rings, Ace=Acentrics, Abc= Aberration cell, Tabc=Total aberration cells, Mn=Micronuclei, Mnc=Micronucleus cells

Tab.1a Differences of effects in chromosome aberration, micronuclei and SCEs in rabbit peripheral blood lymphocytes between two dose levels (F-test)

Index	γ	B	(T $\times$ CO)		(B $\times$ CO)		($\gamma\times$ CO)	CO
			$\gamma\times$ B	T	$\gamma\times$ T	B $\times$ T	B $\times$ T	
D + r	0.97 ⁽²⁾	0.45 ⁽²⁾	0.31 ⁽²⁾	0.35 ⁽²⁾	0.15	0.02	- 0.02	
Ace	0.84 ⁽²⁾	0.04	- 0.22 ⁽²⁾	-0.04	-0.04	0.42 ⁽²⁾	0.06	
Abc	1.73 ⁽²⁾	0.51 ⁽²⁾	0.12	0.36 ⁽²⁾	0.16 ⁽¹⁾	0.41 ⁽²⁾	0.01	
Tabc	1.65 ⁽²⁾	0.60 ⁽²⁾	0.10	0.38 ⁽²⁾	0.17	0.52 ⁽²⁾	- 0.07	
Mn/ ‰	13.58 ⁽²⁾	5.58 ⁽²⁾	1.58 ⁽²⁾	1.78 ⁽²⁾	0.38	0.38	0.28	
Mnc/ ‰	11.55 ⁽²⁾	2.65 ⁽²⁾	1.15 ⁽¹⁾	1.55 ⁽²⁾	0.15	0.15	- 0.15	
SCEs/C	0.24 ⁽²⁾	0.26 ⁽²⁾	0.01	0.15 ⁽²⁾	0.05	0.08	- 0.05	

Note: ⁽¹⁾ $p < 0.05$, ⁽²⁾ $p < 0.01$, $\gamma\times$ B, $\gamma\times$ T, B $\times$ T, represent the interaction between γ and benzene, γ and toluene, benzene and toluene respectively, etc.

2.2 Chromosome aberration of rabbit bone marrow cells

The frequencies of chromosome aberration in rabbit bone marrow cells in all 8 test groups were higher than that in the control (Tab.2; $p < 0.01$). The frequencies of acentric, aberration cells and total aberration induced by γ -rays, benzene and toluene at high level were significantly higher than those at low level, which indicated the three agents could all induced chromosome aberrations.

Tab.2 Frequencies of chromosome aberration in rabbit bone marrow cells

Test groups	Dose levels				Chromosome aberrations/%			
	γ	B	T	CO	D + r	Ace	Abc	Tabc
1	1	1	1	1	0.30	2.75	3.05	3.25
2	1	1	2	2	0.20	2.60	2.80	2.90
3	1	2	1	2	0.20	2.50	2.70	2.80
4	1	2	2	1	0.20	2.15	2.35	2.60
5	2	1	1	2	0.20	0.95	1.15	1.70
6	2	1	2	1	0.10	0.95	1.05	1.45
7	2	2	1	1	0.05	0.90	0.95	1.25
8	2	2	2	2	0.05	0.78	0.83	1.11
Control					0.00	0.35	0.35	0.60

Note: B=Benzene, T=Toluene; D+r=Dicentrics+rings, Ace=Acentrics, Abc= Aberration cell. Tabc=Total aberration cells

Tab.3a Differences of effects in chromosome aberrations in rabbit bone marrow cells between two levels (F-test)

Index	γ	(T $\times$ CO)		T	(B $\times$ CO)		CO
		B	$\gamma \times B$		$\gamma \times T$	$\gamma \times CO$	
D + r	0.13 ⁽¹⁾	0.08	-0.03	0.05	0.00	0.05	0.00
Ace	1.61 ⁽²⁾	0.23 ⁽²⁾	0.12	0.16	0.10	-0.08	-0.02
Abc	1.73 ⁽²⁾	0.31 ⁽²⁾	0.10	0.21 ⁽²⁾	0.10	-0.03	-0.02
Tabc	1.51 ⁽²⁾	0.39 ⁽²⁾	- 0.01	0.24 ⁽²⁾	0.04	0.07	0.01

Note: ⁽¹⁾ $p < 0.05$ ⁽²⁾ $p < 0.01$, $\gamma \times B$, $\gamma \times T$, $B \times T$, represent the interaction between γ and benzene. γ and toluene, benzene and toluene respectively, etc.

However, F-test showed that the interactions among γ -radiation, benzene and toluene were not significant ($p > 0.05$) under the present test conditions. The differences of various effects between two concentrations for CO were much smaller and within the permissible error ($p > 0.05$), which indicated the frequencies of chromosome aberration in bone marrow cells were not affected by CO.

2.3 Effects on sex gland

The effects of agents on sex gland are listed in Tab.3. The significance tests showed that all the four agents could obviously induce certain effects on gland (Tab.3a). Even if all the agents were at low level, the ratio of aberrant sperms was significantly elevated as compared with that of the control group ($p < 0.01$). Gamma radiation, benzene and CO could all decrease testis weight index and number of sperms, and increase the ratio of aberrant sperms ($p < 0.01$). Benzene had negative influence on testis weight index ($p < 0.01$). There were significant interactions between gamma radiation and toluene exposure for decreasing testis weight index and increasing the ratio of aberrant sperms. It should be pointed out, in particular, that CO coupled with other three agents exposure had effects on sex gland.

Tab.3 Effects on rabbit sex gland ($\bar{x} \pm s$)*

Test group	Dose levels				Testis weight index/%	No of sperms / $\times 10^4$ mg	Aberrant rate sperms/%
	γ	B	T	CO			
1	1	1	1	1	0.11 $\pm$ 0.44	2.61 $\pm$ 3.30	13.14 $\pm$ 3.90
2	1	1	2	2	0.17 $\pm$ 0.02	6.89 $\pm$ 3.16	6.69 $\pm$ 0.76
3	1	2	1	2	0.11 $\pm$ 0.02	2.10 $\pm$ 2.80	10.57 $\pm$ 2.56
4	1	2	2	1	0.13 $\pm$ 0.03	3.45 $\pm$ 1.67	8.01 $\pm$ 1.37
5	2	1	1	2	0.18 $\pm$ 0.03	6.36 $\pm$ 1.96	5.43 $\pm$ 0.61
6	2	1	2	1	0.16 $\pm$ 0.02	7.16 $\pm$ 3.99	5.37 $\pm$ 0.68
7	2	2	1	1	0.12 $\pm$ 0.04	(2.45)*	6.29 $\pm$ 0.82
8	2	2	2	2	0.16 $\pm$ 0.04	11.89 $\pm$ 9.14	5.32 $\pm$ 2.51
Control					0.14 $\pm$ 0.03	7.73 $\pm$ 4.62	3.73 $\pm$ 1.13

Note:*Owing to an unexpected loss of experimental data, the number here was an estimation of analysis with orthogonal design method

Tab.3a Differences in effects on rabbit sex gland between two levels (F-test)

Index	γ	B	(T $\times$ CO)		(B $\times$ CO)		($\gamma \times$ CO)	
			$\gamma \times B$	T	$\gamma \times T$	B $\times$ T	CO	
Testis weight index/%	0.03 ⁽¹⁾	0.03 ⁽¹⁾	-0.01	-0.03 ⁽¹⁾	-0.02 ⁽¹⁾	0.01	-0.02 ⁽¹⁾	
No of sperms/ $\times 10^4$ mg	-3.25 ⁽¹⁾	0.73	1.24	-3.92 ⁽¹⁾	1.10	1.38	-2.84 ⁽¹⁾	
Rate of aberrant sperms/%	4.00 ⁽¹⁾	0.11	0.52	2.51 ⁽¹⁾	2.00 ⁽¹⁾	0.75	1.20 ⁽¹⁾	

Note: ⁽¹⁾ $p < 0.01$; The meanings of other symbols are the same as in Tab.1a

2.4 Effects on peripheral hemogram

The differences in peripheral blood hemogram between different test groups were not significant (Tab.4a). When compared with the control, all other data were not statistically significant, except for an increase in thrombocytes ($p < 0.01$) for group 2 and 5.

Tab.4 Effects on rabbit peripheral hemogram(relative, $\bar{x} \pm s$)*

Test group	Dose levels				WBC	Lymphocytes	Hemoglobin	Thrombocytes
	γ	B	T	CO				
1	1	1	1	1	0.94 $\pm$ 0.02	0.84 $\pm$ 0.25	0.95 $\pm$ 0.11	0.83 $\pm$ 0.28
2	1	1	2	2	1.42 $\pm$ 0.66	1.20 $\pm$ 0.71	1.03 $\pm$ 0.15	1.65 $\pm$ 0.86
3	1	2	1	2	1.17 $\pm$ 0.49	1.00 $\pm$ 0.59	1.02 $\pm$ 0.37	0.65 $\pm$ 0.46
4	1	2	2	1	0.97 $\pm$ 0.48	1.08 $\pm$ 1.04	1.01 $\pm$ 0.13	0.85 $\pm$ 0.53
5	2	1	1	2	1.31 $\pm$ 0.82	0.73 $\pm$ 0.33	1.14 $\pm$ 0.15	1.51 $\pm$ 0.83
6	2	1	2	1	1.18 $\pm$ 0.51	1.08 $\pm$ 0.67	1.01 $\pm$ 0.10	0.84 $\pm$ 0.22
7	2	2	1	1	0.83 $\pm$ 0.25	0.78 $\pm$ 0.29	0.89 $\pm$ 0.08	0.94 $\pm$ 0.34
8	2	2	2	2	1.10 $\pm$ 0.39	1.16 $\pm$ 0.82	1.04 $\pm$ 0.11	0.66 $\pm$ 0.14
Control					1.23 $\pm$ 0.56	1.18 $\pm$ 0.45	1.00 $\pm$ 0.17	0.75 $\pm$ 0.20

Note: *Relative to beginning of the experiment

Tab.4a Differences in the results of rabbit peripheral hemogram between two levels (F-test)

Index	γ	B	(T $\times$ CO)		(B $\times$ CO)		($\gamma \times$ CO)	
			$\gamma \times B$	T	$\gamma \times T$	B $\times$ T	CO	
WBC	0.02	0.20	-0.08	-0.11	-0.04	-0.07	-0.27 ⁽²⁾	
Lymphocytes	0.09	-0.04	0.02	-0.30 ⁽¹⁾	0.07	-0.06	- 0.08	
Hemoglobin	-0.02	0.04	-0.07 ⁽¹⁾	-0.02	-0.01	0.05	-0.09 ⁽²⁾	
Thrombocytes	0.00	0.43 ⁽²⁾	0.06	-0.02	-0.49 ⁽²⁾	-0.06	- 0.25 ⁽²⁾	

Note: ⁽¹⁾ $p < 0.05$, ⁽²⁾ $p < 0.01$, Other symbols are the same as in Tab.1a

F-test indicated that toluene could decrease lymphocytes ($p < 0.05$), and CO could cause an obvious decrease in WBC, hemoglobin and thrombocytes counts, and γ -radiation in combination with toluene exposure could also cause significant decrease in lymphocytes (all were very significant, $p < 0.01$). However, benzene could increase thrombocytes, which remain to be elucidated.

3 Discussion

An important problem in the study of combined effects is to determine the features (antagonism, additivity or synergism) of interaction among investigated agents and the degree of interaction (to be indicated by “interactive factor”). These terms have been defined by UNSCEAR in its 1982 report^[1]. To put in brief words, if S_{com} is the combined effects produced by the agents involved and S_a the sum of effects caused by these agents separately. and $\omega \equiv S_{com}/S_a$ is known as interactive factor, the features of this interaction can be referred to as antagonism, additivity and synergism when $\omega < 1$, $\omega = 1$ and $\omega > 1$.

Although the definitions of interacting factors and the above terms in UNSCEAR 1982 report are aimed at two agents, the concepts relative to these terms are applicable to these situations, in which the number of agents involved are more than two.

In the present study, due to lack of the experimental data about the effects of the above four agents acting alone and also due to the fact that data cannot be directly calculated by orthogonol-design analysis, it is difficult to acquire interacting factors. According to the characteristics of orthogonol layout [$L_8(2^7)$] program, the ω can still be calculated by means of the tests data shown in Tab.1~4.

If E_k represents the difference of a special effect between test group k ($k=1,2,3, \dots, 7$) and group 8 in Tab.1~4, then the E_k is just the increment of combined effects of four (for test group 1) or two agents from low exposure level to high level. Consequently, the E_k can be associated with following equality:

$E_1 = E_\gamma + E_B + E_T + E_{CO} + E_{\gamma \times B} + E_{\gamma \times T} + E_{\gamma \times CO} + E_{B \times T} + E_{B \times CO} + E_{T \times CO}$
where E_i ($i=\gamma, B, T$ and CO) is the increment of the effect of agent i acting alone, and E_{ij} (i and $j=\gamma, B, T, CO; i \neq j$) is one caused by interaction between i and j . Similarly, it is not difficult to understand the following relationships:

$E_2 = E_\gamma + E_B + E_{\gamma \times B}; E_3 = E_\gamma + E_T + E_{\gamma \times T} \dots$

If E_d is the sum of the increment of the effect caused by four agents separately due to increasing exposure level, it can lead to the equality $E_d = E_\gamma + E_B + E_T + E_{CO} = (\sum_{k=2}^7 E_K - E_1)/2$ by making use of these relationships. Because E_1 is the increment of the effect by the four agents on acting simultaneously, hence, ω can be written as $\omega = E_1/E_d$. ω values caused by the four agents were listed in Tab.5.

Tab.5 Certain ω values produced by the four agents

Effect	Peripheral blood lymphocytes						Sex gland		
	D + r	Acc	Abc	Tabc	Mn	SCEs/C	Rate of aberrant sperms	Number of sperms	Testis eight index
ω	2.16	1.58	2.07	2.67	1.31	1.18	5.97	0.65	2.50

All ω values in Tab.5, except the number of sperms, were more than one, which shows that the combined effects caused by γ -rays in combination with the other three agents were mainly synergistic.

It should be pointed out, in particular, that the ω values for dicentric+ring, acentric, aberration cells, total aberration, and testis weight index were more than two, whereas ω for the ratio of aberrant sperms was as high as 5.97.

Previously, when a medical standard against certain agents was made or when effects on human health in a multi-factor environment was analyzed, the materials (or data) provided were usually from studies of the effects of separate agents, and their interactions were not considered. Our present study indicated that effects of pure interactions caused by several agents may be much greater than the sum of individual effects of the agents acted on alone. Consequently, with regard to a multi-factor environment, we must take account of the interacting effects of certain contributing agents.

It is noted that all agents in test group 8 were under the "low-level" condition. The relationship between the concentration of each gas and its permissible value in air can be seen as follows: ratio of the total amount of gas inhalation between the exposure of 2 h a day and the exposure at permissible concentration of 24 h a day is 0.96, 0.65 and 0.65 for benzene, toluene and carbon monoxide respectively. In addition, according to our foregoing chronic γ -rays irradiation experiments in which exposure conditions were same as the present one, changes in cytogenetic effects of γ -rays dose at 0.3 Gy were not obviously seen ($p > 0.05$) when compared with the control. However, the differences in effects between Group 8 and the control were significant. It indicated that we must take account of the effects of combined effects by benzene, toluene and CO when working out protective standards of permissible concentrations of these agents in air in a multi-factor environment where there exist the three gases.

The experimental results showed that CO had no cytogenetic effects, but it could significantly decrease the number of sperms and increase the ratio of aberrant sperms. It has been reported^[10] that CO combined with high temperature exposure could intensify lesion to testis. The present studies indicated that CO combined with γ -rays benzene and toluene had significant synergistic effect on the lesion of sex gland.

References

- 1 United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) Ionizing Radiation: Sources and Biological Effects (Annex L), Report to the General Assembly. Vienna, 1982
- 2 Cross F T, Palmer R F, Filipy R E *et al.* Study of the Combined Effects of Smoking and Inhalation of Uranium Ore Dust, Radon Daughters and Diesel Oil Exhaust Fumes in Hamsters and Dogs. PNL-2744, 1978
- 3 Wang T J, Peng Q Y, Liu Z Q *et al.* Chin J Naut Med (in Chinese), 1998, 5:110-113
- 4 Panel on Monitoring, Panel Hyperbaric and Mixtures, Subcommittee on Submarine Air Quality. *et al.* Submarine Air Quality (Monitoring the in Submarines, Health Effects in Divers of Breathing Submarine Air Under Hyperbaric Condition), Washington D C: National Academy Press, 1988, 60-65
- 5 Zhang H Y, Wang L J, Cai Ping *et al.* Nucl Sci Tech, 1995, 6:246-251
- 6 Zhang H Y, Wang Y X, Wang L J *et al.* J Radiat Res Radiat Proces (in Chinese), 1998, 16:57-61
- 7 Fenech M, Morley A A. Mutat Res, 1985, 147:29-36
- 8 Wang S, Lei H P. Nat Med J China (in Chinese), 1979, 59:402-405
- 9 Zhang H Y, Wang Y X, Wang L J *et al.* Chin J Naut Med (in Chinese), 1997, 4:204-208
- 10 Chen G Y, Zhang Z D, Lu C R *et al.* Occup Med(in Chinese), 1993, 20:330-332

γ 射线照射同时吸入苯、甲苯和 CO 对家兔的复合作用

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摘要 研究了 γ 射线照射同时吸入苯、甲苯和 CO 产生的复合效应,并分析了这四个因素之间相互作用的性质(拮抗、相加或协同)。90 只家兔分成 9 组,按 $L_8(2^7)$ 正交表设计进行四因素二水平的 8 组实验,另一组为对照组。各因素的两种暴露水平分别是: γ 射线为 0.0075Gy/d 和 0.0375Gy/d; 苯为 $40 \pm 15 \text{mg/m}^3$ 和 $182 \pm 33 \text{mg/m}^3$; 甲苯为 $90 \pm 30 \text{mg/m}^3$ 和 $407 \pm 68 \text{mg/m}^3$; CO 为 $93 \pm 4 \text{mg/m}^3$ 和 $278 \pm 8 \text{mg/m}^3$ 。暴露实验在密闭舱内进行,每天 2h,每周 5d,持续 8 周。对实验结果用方差分析和组间比较进行了处理。结果: (1) 相互作用因子,即四个因素的联合作用效应与四个因素单独作用产生的效应总和的比值(ω),对淋巴细胞的双着丝点加环、无着丝粒、畸变细胞、总畸变、微核及 SCEs/C 分别为 2.16、1.58、2.07、2.67、1.31 和 1.18。对畸形精子率则高达 5.97。这些数值显示各因素之间的相互作用主要是协同作用($\omega > 1$),但苯和 γ 射线结合对淋巴细胞无着丝粒为拮抗作用。(2) γ 射线、苯、甲苯和 CO 四个因素都引起睾丸重量指数降低; γ 射线、甲苯和 CO 能引起精子数减少和畸形精子率增高; γ 射线与甲苯对降低睾丸重量指数和增高畸形精子率有显著的协同性交互作用。(3) CO 能导致白细胞总数、血小板及血红蛋白显著减少,甲苯能使淋巴细胞减少。(4) γ 射线、苯和甲苯对诱发某些生物效应具有很显著的协同作用; CO 在与其它三个因素同时作用时对性腺能引起显著的影响。

关键词 γ 射线, 苯, 甲苯, CO, 复合效应, 相互作用因子

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