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RADIOPROTECTIVE EFFICACY OF CYSTEAMINE

by

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The radioprotective efficiency of cysteamine has been investigated in different animal species since its discovery by BACQ (BACQ et coll. 1953, GROS et coll. 1955, GEREBTZOFF et coll. 1954, DEVIK et coll. 1955, MAISIN et coll. 1955, ARMELLINI et coll. 1958, FUMAGALLI et coll. 1958 and CHATTERJEE et coll. 1959). The radioprotective efficacy of a 150 mg/kg bodyweight dose of cysteamine against a lethal dose (800 r) of radiation was reported in a previous publication from this centre; the intervals varied from zero hour to 30 days following irradiation (DE et coll. 1961), with the mitotic index of rat bone marrow cells as the reference system. The purpose of the present work was to study with the same criterion the ability of cysteamine to modify the effects of varying doses of whole body radiation ranging from 400 r to 800 r. Bone marrow cells were selected by reason of their constant supply of physiologically active cells (MAXIMOW et coll. 1952), their increased incidence of mitosis (THORELL 1947), and their highly radiosensitive behaviour (BLOOM 1948).

Material and Method. The experiments were conducted on inbred Indian albino rats of both sexes and of the same strain, and with the same average bodyweight (about 125 g). The whole body radiation doses used were 400 r, 500 r, 600 r, 700 r and 800 r. Each radiation dose group consisted of normal controls, irradiated only, which were given the whole body radiation dose from

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Table

Evaluation of radioprotective effect of cysteamine as a function of dose range

	Mitotic index %			Protection % $\left(\frac{P-R}{N-R}\cdot 100\right)$	Damage % $\left(\frac{N-R}{N}\cdot 100\right)$	Value of t between N & P	Significance at	Value of t between R and P	Significance at
	Normal control (N)	Irradiated only (R)	Protected & irradiated (P)						
800 r	1.39 ±.062	0.52 ±.093	0.63 ±.060	13	63	33.0	0.1 %	4.1	0.1 %
700 r	1.37 ±.078	0.56 ±.046	0.80 ±.074	30	59	24.7	0.1 %	14.1	0.1 %
600 r	1.40 ±.107	0.62 ±.065	1.09 ±.093	60	56	10.3	0.1 %	17.4	0.1 %
500 r	1.40 ±.094	0.67 ±.070	1.21 ±.100	74	52	7.9	0.1 %	20.8	0.1 %
400 r	1.39 ±.080	0.75 ±.060	1.38 ±.110	98	46	0.5	Not significant	21.0	0.1 %

a 250 kV generator (1.5 mm Cu HVL), and the protected and irradiated animals in which the radiation was administered immediately after the intraperitoneal administration of 150 mg/kg bodyweight of cysteamine. Each series for each dose group consisted of three animals and the whole experiment involved 45 animals. All the animals were sacrificed on the 10th day following irradiation, in line with the earlier findings of De et coll. (1961). The results of the mitotic index have been expressed as a percentage: mitotic cells 100/ total nucleated cells. There was one mitotic index comprising about 2 000 nucleated, randomly counted bone marrow cells for each animal. The mitotic indices determined are given in the table.

The following formulae were used for arriving at the protection and inhibition percentages:

$$\text{Percentage protection} = P—R/N—R \cdot 100$$
$$\text{Percentage inhibition} = N—R/N \cdot 100$$

where P represents the mitotic index in protected and irradiated animals, R in animals irradiated only and N in normal controls. Protection % and inhibition % are included in the last two columns of the table.

Discussion

The reference system employed for this study represents the growth manifestation of haemopoietic cells. It was found in previous experiments (De et coll. 1961) that the maximum inhibitory effect occurred within half an hour following irradiation, after which the process was that of gradual recovery

till the 10th day. In lethally irradiated animals without protection the inhibitory effect begins to gain ascendancy after the 10th day till the animal dies. This second phase of radiation action in protected animals, however, starts from the 10th day and lasts only till the 15th day, after which the recovery process again becomes predominant. This set of experiments afforded an opportunity of studying the recovery process, and the effect of cysteamine on such recovery, with irradiations ranging from sublethal to lethal doses. It may be seen from the table that the percentage of inhibition bears a direct relationship to the radiation dosage, whereas the percentage of protection bears an inverse relationship to it. The protection and inhibition percentages as a result are inversely proportional. The percentage inhibition was 46 and the percentage protection was 98 at the lowest dose used (400 r). This means that the cysteamine at some point exerted an influence whereby the animal had fully recovered from the effect of radiation as far as this criterion is concerned. However, with 800 r the percentage inhibition was 63, and as such even the effect of cysteamine was not able to give more than 13 per cent protection. This leads to the conclusion that within the dose ranges studied the radioprotective efficiency of cysteamine is inversely proportional to the radiation dosage.

SUMMARY

A study of the efficacy of 150 mg/kg bodyweight cysteamine in modifying the effects of whole body radiation doses ranging from 400 r to 800 r is reported. The mitotic index of rat bone marrow cells was used as the biologic reference system. The conclusion is reached that the efficacy of cysteamine is inversely proportional to the radiation dosage.

ZUSAMMENFASSUNG

Die Wirksamkeit einer Verabreichung von 150 mg/kg Cysteamin bezüglich seiner Fähigkeit die Effekte einer Gesamtbestrahlung von 400 bis 800 r zu modifizieren wird besprochen. Der Mitosenindex des Knochenmarkes der Ratte wurde als biologischer Gradmesser benutzt. Die Schlussfolgerung ist, dass die Wirksamkeit des Cysteamins umgekehrt proportional zur Strahlendosis ist.

RÉSUMÉ

Les auteurs ont étudié l'influence de 150 mg de cystéamine par kg de poids corporel sur les effets de l'irradiation corporelle totale par des doses comprises entre 400 et 800 r. L'indice mitotique des cellules de la moelle osseuse du rat a été utilisé comme système de référence biologique. La conclusion est que l'efficacité de la cystéamine est inversement proportionnelle à la dose de radiation.

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