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COMBINED EFFECT OF ROENTGEN IRRADIATION AND RADIOSTRONTIUM ON THE HAEMATOPOIETIC TISSUES AND THE DEVELOPMENT OF LYMPHOMA IN MICE

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Radiation from an external roentgen source and internal ^{90}Sr each causes damage to the haematopoietic tissue. This is a relatively well known phenomenon and in the long run may involve, inter alia, the risk of leukaemia. The external irradiation is of brief duration and impinges upon the whole of the haematopoietic tissue simultaneously and with roughly similar intensity. Radiostrontium absorbed initially circulates and so affects all haematopoietic tissue. After strontium has accumulated in the skeleton, the radiation will be concentrated to the bone marrow during a lengthy period. Leukaemias induced by ^{90}Sr in mice also derive often from the bone marrow (WATANABE 1958, NILSSON 1971), whereas, when induced by fractionated external irradiation, they usually start in the thymus (KAPLAN 1947, JÄRPLID 1968). It would appear to be a realistic view that in certain situations individuals may be subjected to a combination of these forms of irradiation. The effects of such combined irradiation are, however, unknown, which is the reason for the present investigation with respect to changes in the haematopoietic tissue and the occurrence of leukaemia.

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Table 1

Haematopoietic tissues. Survey of experiment

No. of animals	Roentgen irradiation	Injection of ^{90}Sr/g body weight	Autopsy, time after last treatment
30 (controls)	—	—	5–97 days
104 (group X)	4×140 R	—	4–100 days
104 (group XS)	4×140 R	0.2 μCi	4–100 days

Material and Methods

Female CBA mice, aged 30 ± 3 days, were used. The total dose of whole-body irradiation was given in four equal fractions every fifth day. The animals were irradiated in groups of ten in a plastic 'wheel' as described earlier (JÄRPLID 1968). The roentgen apparatus used, Müller MG 300, was operated at 260 kV, 9.5 mA, filter 0.5 mm Cu + 0.5 mm Al. An extra filter of Cu was used with a HVL 1.9 mm Cu at the periphery and a HVL 2.2 mm Cu at the centre. The focal distance was 45 cm and the dose rate 74 R/min. $^{90}Sr(NO_3)_2$ was injected intraperitoneally and, in the combined experiments, within five hours after the last fraction of external irradiation. For blood examination animals were anaesthetized with ether and blood samples were obtained with a Pasteur pipette from the medial venous plexus of the eye. The total numbers of leucocytes were counted in a Bürker chamber by conventional manual methods. For histologic examination haematopoietic tissues were fixed in Stieve's fluid (ROMEIS 1948), prepared by conventional histologic technique and stained with Ehrlich haematoxylin and eosin.

The day for (last) treatment was called day 0.

Haematopoietic tissues. In this experiment 208 mice were given fractionated irradiation with a total dose of 560 R and were divided into two equal groups (Table 1). From one of these groups (group X) 8 animals were selected at random, subjected to blood examination, and killed at intervals of 4, 8, 11, 17, 21, 24, 28, 32, 39 51, 60, 78, and 100 days after the last fraction. The animals in the other group (group XS) were injected in addition with 0.2 μCi ^{90}Sr/g body weight. Eight mice from this group were then selected at random, subjected to blood examination and killed at intervals of 4, 8, 12, 15, 20, 25, 29, 35, 40, 50, 57, 76 and 100 days after the injection of ^{90}Sr. Thirty mice served as an untreated control group. Eight animals from this group were selected at random and handled as above at intervals of 5, 20, 40, 58 and 97 days after the last

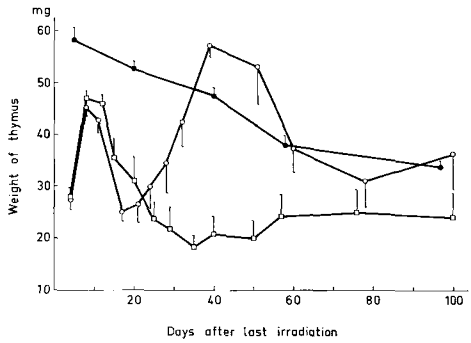

Fig. 1. Weight of thymus. Untreated controls (●———●). External irradiation, 4 × 140 R (○———○). External irradiation combined with ^{90}Sr, 0.2 μCi/g body weight (□———□). n for each sample = 8. Mean ± SE.

irradiation of the X and XS groups. At the autopsy the thymic lobes were dissected, weighed separately and fixed for histologic examination. The spleen was also weighed and fixed together with femur and sternum.

Survival time and lymphoma incidence. A survey of different parts of this experiment is given in Table 3. A total of 370 animals was used. In the first part (A—C, E) 170 mice were given 4 × 140 R and then injected with ^{90}Sr in various doses (0, 0.1, 0.2 and 0.4 μCi/g body weight). In the second part of the

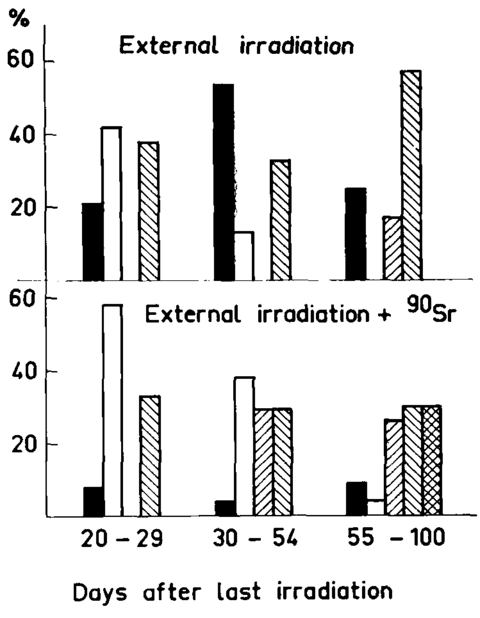

Fig. 2. Thymus. Incidence of different histologic appearances. External irradiation, 4 × 140 R, and external irradiation combined with ^{90}Sr, 0.2 μCi/g body weight. Normal histology ■, Bilateral depletion □, Bilateral regeneration ▨, Histologic asymmetry ▧, Lymphoma ▩.

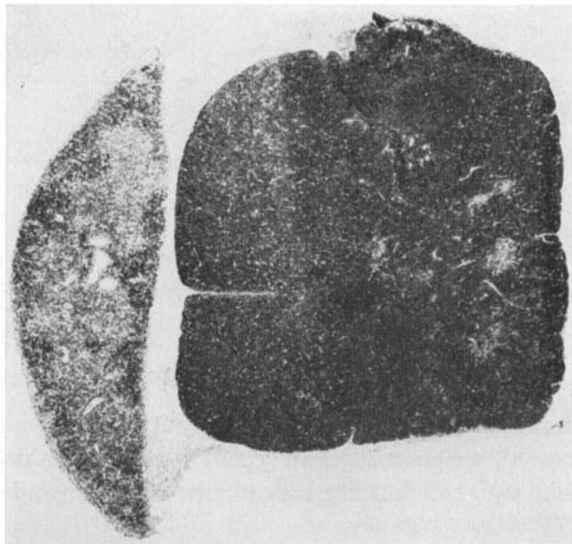

Fig. 3. Asymmetric thymus 25 days after combined treatment with external irradiation, 4 × 140 R, and ^{90}Sr, 0.2 μCi/g body weight. Left lobe, lymphocyte depletion with cortical thinning, weight 6.0 mg. Right lobe, regenerated with small medullary areas, weight 13.7 mg. H & E, × 20.

experiment 50 mice (F) received 4 × 70 R and another 50 mice (G) 4 × 35 R. Then all these hundred animals (F, G) were injected with 0.2 μCi ^{90}Sr/g body weight. Fifty mice (H) were not irradiated but injected with 0.2 μCi ^{90}Sr/g body weight at an age of 45 ± 3 days, which corresponds to the age of the irradiated mice at the end of irradiation. Another 50 mice (D) were thymectomized 5 to 7 days before the start of irradiation at about 30 days of age. These animals received 4 × 140 R and then 0.2 μCi ^{90}Sr/g body weight. Thymectomy was performed according to the method described by Sjödin et coll. (1963).

All animals were autopsied as soon as possible after their natural death. To get fresh specimens for haematology and histology some animals were killed in a moribund state. The weight of thymus and spleen was noted and specimens from thymus, spleen, external lymph nodes, sternum and femur were fixed for histologic examination.

Results

Haematopoietic tissues

Thymus. The changes in total weight of the thymus after fractionated irradiation (group X) and after additional injection of ^{90}Sr (group XS) are illustrated in Fig. 1. In both groups the first phase of regeneration had started by day 4. Immature lymphoid cells with a lymphoblast-like appearance predominated in the thymic cortex. At the maximum of this regeneration phase on days 8 to 12

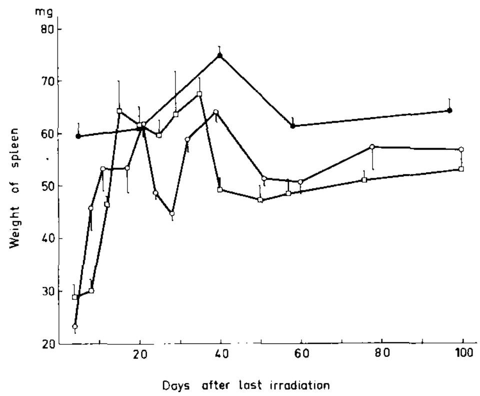

Fig. 4. Weight of spleen. Untreated controls (●———●). External irradiation, 4×140 R (○———○). External irradiation combined with ^{90}Sr, 0.2 $\mu Ci/g$ body weight (□———□). n for each sample = 8. Mean ± S E.

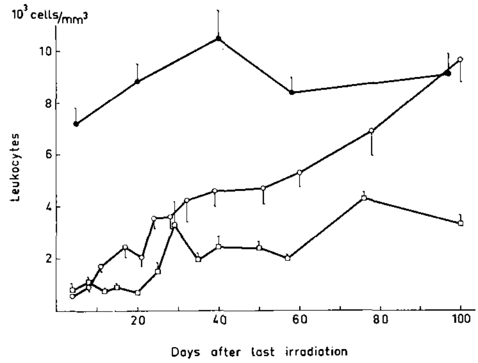

Fig. 5. Total number of leukocytes in peripheral blood. Untreated controls (●———●). External irradiation, 4×140 R (○———○). External irradiation combined with ^{90}Sr, 0.2 $\mu Ci/g$ body weight (□———□). n for each sample = 8. Mean ± S E.

the histologic appearance of the thymus was almost normal. In both groups the thymus thereafter again decreased in weight as a result of a new and bilateral lymphocyte depletion (second phase of lymphocyte depletion, JÄRPLID 1968) in the thymic cortex, which thereby acquired an irregular, thin and less dense appearance (cortical thinning, Fig. 3, left lobe).

In the period 20 to 29 days the thymus in the XS group was characterized by a high incidence (58 per cent) of bilateral lymphocyte depletion, which resulted in a further decrease in weight of the organ (Figs 1, 2). In the X group a second phase of regeneration set in with a new increase in weight and a higher incidence of histologically normal thymus than in the XS group (21 and 8 per cent respectively). The incidence of histologic asymmetry (i.e. one lobe had a normal histologic appearance or was in a regeneration phase, while the other lobe was the site of depletion of different degrees, Fig. 3, JÄRPLID 1968) was about the same in the two groups (33 to 38 per cent). No case of bilateral symmetrical regeneration was seen during this period.

During the period 30 to 54 days the thymus of the X group had its maximum in weight and in incidence of normal histology (54 per cent, Figs 1, 2). The incidence of bilateral lymphocyte depletion was low (13 per cent). In the XS group the mean weight of the thymus had its minimum in this period. In 67 per cent of the animals the thymus exhibited morphologically bilateral lymphocyte depletion or regeneration. The incidence of normal thymus was very low (4 per cent).

Table 2

Individual cases of lymphoma in mice killed at monthly intervals (n for each sample = 8) after combined treatment with fractionated irradiation (4× 140 R) and ^{90}Sr (0.2 µCi/g body weight)

Time after last irradiation (days)	Total number of leukocytes/mm³ blood	Haematopoietic tissues involved		
		Thymus	Bone marrow	Spleen
57	900	+	–	–
76	3 900	+	+	+
76	1 400	+	–	–
100	39 800	+	+	+
100	2 600	+	–	–
100	3 700	+	–	–
100	4 900	+	+	+
100	3 100	+	–	–

During the last period investigated (55 to 100 days) the thymus in the X group had a relatively normal mean weight though the incidence of normal thymus had decreased again (Figs 1, 2). Instead in 54 per cent of the animals the thymus was asymmetrical mainly with one normal lobe and one lobe in regeneration. No case of lymphoma appeared in this group.

In the XS group the thymic weight was rather low. Histologically three thymic appearances predominated, bilateral regeneration (26 per cent), asymmetry (30 per cent) and lymphoma (30 per cent). In only 9 per cent of cases was the thymus histologically normal.

Spleen. The changes in weight of the spleen are illustrated in Fig. 4. Both in groups X and XS the histologic appearance of the red pulp was initially characterized by a moderately increased extramedullary haematopoiesis. This compensatory haematopoiesis persisted for about three weeks in the X group and during the entire observation period in the XS group. Cells from both the erythroid, myeloid and the megakaryocytic cell series successively replaced the initially predominating red cell precursors in this haematopoiesis.

In both groups the number of lymphocytic cells decreased in the periphery of the spleen follicles. In this region accumulations of larger lymphoid cells (germinal centres) appeared after about three weeks in the X group and about two months in the XS group.

Bone marrow. The acute radiation injury was histologically characterized by dilatation of sinusoids, haemorrhage and reduced cellularity. The degree of these

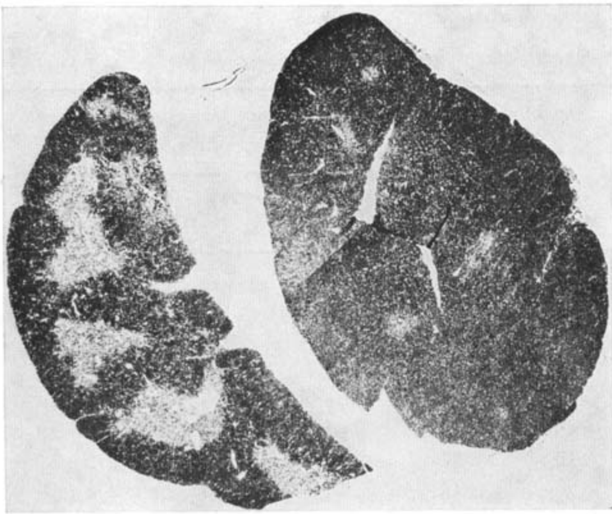

Fig. 6. Thymus. One hundred days after combined treatment with external irradiation, 4 × 140 R, and ^{90}Sr, 0.2 μCi/g body weight. Unilateral lymphoma of right lobe, weight 28.3 mg. Left lobe normal, weight 10.4 mg H & E, × 20.

changes varied between different sections of the marrow from a moderate degree of cellular depletion to large haemorrhages with only a few scattered haematopoietic cells. During this cellular depletion period, cells belonging to the granulocytic series predominated in the marrow. The injury was most severe during the period 4 to 8 days after external irradiation and 4 to 20 days after combined treatment. In the X group focal regeneration led to a relatively normal histologic appearance by day 17. In the XS group, however, the regeneration was delayed and a successively increased cellularity during the period 20—29 days led to a relatively normal histology of the marrow by days 35, 40 and 50. Thereafter, however, and during the rest of the observation period, the cellularity of the bone marrow of the femur was again moderately decreased at the same time as the sternal bone marrow remained relatively normal.

Peripheral blood. After external irradiation the total number of leucocytes increased successively from a minimum at day 4 to a normal mean value at day 100. In the group treated with combined external and internal radiation, however, the number of leucocytes was below normal during the whole observation period (Fig. 5).

Development and incidence of lymphoma

In mice which were killed periodically 4 to 100 days after treatment, cases of lymphoma appeared only after combined treatment with both external irradiation and ^{90}Sr (Table 2). All the eight cases observed were of the thymic lymphoma

Table 3

Incidence of lymphoma and latency time for lymphoma development

No. of mice		Dose (R)	Dose of ^{90}Sr (μCi/ g body weight)	Incidence of lymphoma, per cent			Mean latency time (days) ±SE	
				Thymic	Non-thymic	Total	Thymic	Non-thymic
A	48	4×140	—	37	17	54	210±11	233±33
B	48	4×140	0.1	60	13	73	177± 9	199±17
C	46	4×140	0.2	74	13	87	164± 9	179±17
D	50	4×140 (th-x)*	0.2	—	28	28	—	191±15
E	28	4×140	0.4	68	3	71	184±16	134
F	50	4× 70	0.2	46	16	62	255±27	257±31
G	50	4× 35	0.2	18	32	50	279±40	275±22
H	50	—	0.2	2	12	14	181	278±51
	370							

* th-x = thymectomy

type, which is usually seen after fractionated leukaemogenic irradiation (Kaplan 1947, Järplid 1968). Of 5 cases localized only to the thymus 3 were unilateral (Fig. 6). Three cases were generalized with lymphoma changes also in bone marrow and spleen. Seven out of eight mice with lymphoma changes had a low or rather low number of leukocytes in the peripheral blood.

In those groups of the animals which were used for determining survival time and tumour incidence, the cases of lymphoma were divided into two main groups according to the localization of the predominating changes, thymic lymphomas and non-thymic lymphomas.

Thymic lymphoma. The thymus was generally much enlarged (mean weight 407 ± 23 mg) and the two lobes were often indistinguishable as a result of accretion. In some cases the changes were localized only to the thymus. Often, however, extra-thymic haematopoietic tissues were also affected. Tumour cells were then predominatly localized to the red pulp of the spleen, with or without enlargement of this organ, and to the bone marrow and lymph nodes (generalized thymic lymphoma).

Non-thymic lymphoma. Lymphoma appeared in extra-thymic haematopoietic tissues with slight or no enlargement of the thymus (mean weight 23 ± 3 mg). The spleen, the lymph nodes or both were generally the site of lymphoma

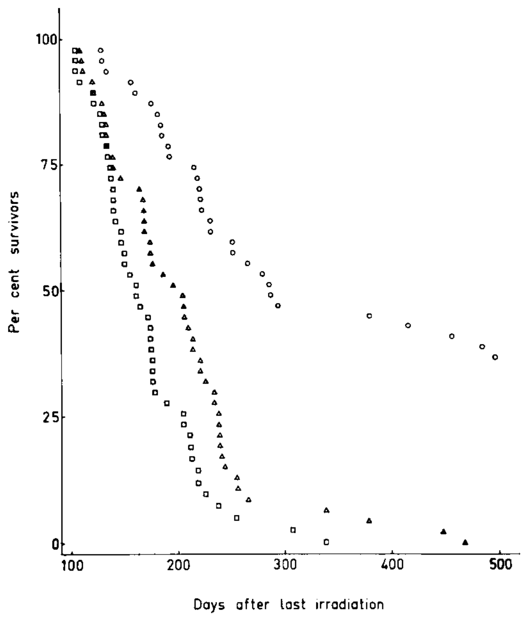

Fig. 7. Survival time for mice. External irradiation, 4 × 140 R (○——○). External irradiation combined with ^{90}Sr, 0.1 μCi/g (△——△) and 0.2 μCi/g body weight (□——□).

changes and often enlarged, and a heavy proliferation of lymphoid tumour cells was seen in the bone marrow. In the case of enlargement of the thymus the lymphoma changes were primarily localized to the peripheral parts of the thymic lobes, giving the impression of being metastases.

Lymphomas which were localized around the vertebral column, predominantly around the lumbar vertebrae, were seen after treatment with reduced doses of external irradiation and 0.2 μCi ^{90}Sr/g body weight. These tumours often reached a size of a pea to a hazelnut. They seemed to develop from the bone marrow of the vertebrae and they sometimes infiltrated the vertebral canal but dit not affect the bone tissue proper.

Incidence of lymphoma. The incidence of lymphoma in different parts of the experiment is shown in Table 3. The spontaneous incidence of lymphoma in this strain is about one per cent (NILSSON 1971). After treatment with 0.2 μCi ^{90}Sr/g body weight thymic lymphoma appeared in 2 per cent of animals and non-thymic lymphoma in 12 per cent. In the group which received 4 doses of 140 R and various doses of ^{90}Sr the incidence of thymic lymphoma after only fractionated irradiation (37 per cent) was doubled after additional treatment with 0.2 μCi ^{90}Sr/g body weight (74 per cent). An addition of 0.1 μCi ^{90}Sr resulted in 60 per cent lymphoma and an addition of 0.4 μCi ^{90}Sr in 68 per cent

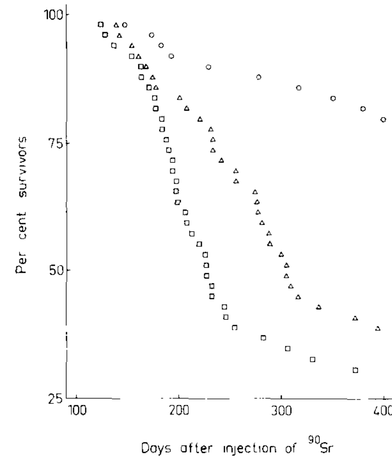

Fig. 8. Survival time for mice. Treatment with ^{90}Sr, 0.2 μCi/g body weight (○———○). External irradiation 4×35 R (△———△) and 4×70 R (□———□) plus ^{90}Sr, 0.2 μCi/g body weight.

lymphoma of the thymus. The incidence of non-thymic lymphoma after external irradiation (17 per cent) decreased after additional treatment with ^{90}Sr (to 3 per cent after an addition of 0.4 μCi). After thymectomy the incidence of non-thymic lymphoma increased from 13 to 28 per cent.

If the roentgen dose was lowered (from 4 × 140 R to 4 × 70 R) and the dose of strontium remained at 0.2 μCi/g body weight, the incidence of thymic lymphoma decreased from 74 to 46 per cent while the incidence of non-thymic lymphoma slightly increased from 13 to 16 per cent. If, however, the dose of external irradiation was lowered further (4 × 35 R), the incidence of non-thymic lymphoma was doubled (from 16 to 32 per cent) at the same time as the thymic lymphoma incidence decreased from 46 to 18 per cent (Table 3). Lymphomas around the vertebral column appeared in six mice (12 per cent) which had received 4 × 70 R + ^{90}Sr and in ten mice (20 per cent) after treatment with 4 × 35 R + ^{90}Sr. Among these mice 3 and 4, respectively, had at the same time a thymic lymphoma.

Latency time. No significant difference in mean latency time appeared between thymic lymphoma and non-thymic lymphoma (Table 3). However, there was a tendency for the latency time of both these tumours to decrease after additional treatment of irradiated (4 × 140 R) mice with ^{90}Sr.

Survival time. The survival time for mice in different groups is shown in Figs 7 and 8. Combined treatment with roentgen irradiation and ^{90}Sr led to a reduced survival time in comparison to treatment with only external irradiation or only ^{90}Sr.

Discussion

Thymus. The diphasic regeneration process in the thymus after external whole-body irradiation has been described earlier by JÄRPLID (1968). A similar regeneration process in the thymus has been found after injection of ^{90}Sr in different doses (JÄRPLID 1973). After a combination of these forms of irradiation no second regeneration phase occurred in this experiment (Fig. 1). Instead the second depletion phase was accentuated and prolonged, so that the weight of the thymus did not attain normal value during the entire observation period. Histologically the thymus was characterized during this second depletion phase by a high incidence of bilateral lymphocyte depletion and low incidence of normal appearance. Earlier experiments have shown that protection of active bone marrow under external irradiation or injection of viable bone marrow cells after such irradiation promotes the regeneration of the thymus and prevents the occurrence of the second depletion phase (KAPLAN et coll. 1953, JÄRPLID 1968). The role of the protected bone marrow in this respect is not entirely established, but the existing data may indicate that it furnishes stem cells which can repopulate the thymus and facilitate its regeneration (POPP 1961, FORD & MICKLEM 1963, METCALF 1966, WALLIS et coll. 1966). This suggests that the absence of recovery of the thymus in this experiment may be associated with a ^{90}Sr induced deficiency of bone marrow cells which are competent to repopulate the thymus.

As from day 20, cases of histologic asymmetry of the thymus occurred in both treatment groups (Figs 2, 3). After external irradiation alone the incidence of asymmetry during the different observation periods was 38, 33 and 54 per cent respectively. Inspection and biopsy of the thymus indicate that unilateral thymic changes can alternate from one lobe to the other within the same thymus (reversed asymmetry, JÄRPLID 1968). The asymmetry thus appears to be an expression of instability within the thymus. In this experiment the incidence of asymmetry was highest during the period immediately before the manifestation of lymphoma, which may also indicate that asymmetry and thymic lymphoma are in some way associated phenomena (JÄRPLID 1968).

After external irradiation and strontium treatment the incidence of asymmetry from day 20 to 100 was around 30 per cent (Fig. 2). From day 30 to 54 there was an increase in the incidence of bilateral regeneration, and during the last part of the observation period, from day 55 to 100, lymphoma also appeared, so that the incidences of bilateral regeneration, asymmetry and lymphoma were then of similar magnitude (26 to 30 per cent). These various changes were seen in 86 per cent of the animals in this last period and the final incidence of thymic lymphoma was 74 per cent (mean latency time 164 days, Table 3). It thus appears probable that, after this combined treatment, bilateral regeneration in small thymic lobes and asymmetry may be of the same significance for the occurrence of these thymic lymphomas as are unilateral thymic changes (asymmetry) for the occurrence of thymic lymphoma after external irradiation alone (JÄRPLID 1968).

Bone marrow. The bone marrow changes after fractionated external irradiation conformed with those described earlier (FLIEDNER et coll. 1961, JÄRPLID 1968). The delayed regeneration seen after combined treatment is presumably caused by radiation from strontium accumulated in the bone. The fact that during the later part of the observation period the sternum and femur differed in respect of cellularity is probably attributable to the variation within different bones and sections of bone of the dosage of radiation absorbed in the bone marrow owing to differences in metabolism, geometry etc. (NILSSON 1962).

Spleen. The increased extramedullary haematopoiesis in the red pulp of the spleen persisted for about three weeks after external irradiation and during the entire observation period after combined treatment. This increased haematopoiesis, which has also been seen for long periods after treatment with only ^{90}Sr (NILSSON 1962), is compensatory for the bone marrow injury.

Peripheral blood. The low number of leucocytes in the peripheral blood during the entire observation period after combined treatment also probably reflects the bone marrow injury by ^{90}Sr (NILSSON 1962).

Lymphoma development. The incidence of thymic lymphoma fell with the roentgen dose if the strontium dose was maintained constant (0.2 μCi/g body weight, Table 3). If the animals were not roentgen-irradiated but merely injected with 0.2 μCi strontium, the incidence of thymic lymphoma was 2 per cent, which cannot be said to deviate from the observed spontaneous incidence in this mouse strain (NILSSON 1971). The injury caused to the thymus by this dose of ^{90}Sr appears also to be relatively insignificant (JÄRPLID 1973).

As previously mentioned, lymphomas induced by ^{90}Sr derive chiefly from the bone marrow, but those induced by fractionated external radiation usually start in the thymus. Treatment of externally irradiated animals with ^{90}Sr, however, in some cases caused a twofold increase in the incidence of thymic lymphoma. It has been mentioned above that the absence of thymic regeneration may be due to a lack of competent bone marrow cells. It is possible, too, that the radiation injured thymus is fed with bone marrow cells which, through radiation from strontium, have become defective or modified and which may conceivably be potentially malignant. For chromosomally abnormal haematopoietic cells have proved capable of survival in the thymus but not in bone marrow or spleen of leukemogenically irradiated mice (ILBERRY et coll. 1963, JONEJA & STICH 1965).

After treatment with 4 × 140 R externally or 0.2 μCi ^{90}Sr internally the incidence of non-thymic lymphoma was 17 and 12 per cent respectively (Table 3). The incidence induced by 4 × 140 R (17 per cent) was decreased by injection of strontium. Thus, with an addition of 0.4 μCi strontium, the incidence fell to 3 per cent, probably because the radiation injury to the bone marrow was then too great. NILSSON (1971), in fact, found that the majority of non-thymic lymphomas induced by strontium start in the bone marrow and that, in the dose range 0.2 to 0.8 μCi, the incidence of such bone marrow lymphomas is inversely related to the injected dose. The incidence of non-thymic lymphomas found after treatment with 0.2 μCi ^{90}Sr (12 per cent) could be raised (to 32 per cent) only if the treatment was combined with the small roentgen dose here tested (4 × 35 R). The degree of damage and regeneration so obtained in the bone marrow manifestly favoured the occurrence of lymphoma.

The combination of strontium and a relatively low dose of roentgen induced lymphoma around the vertebrae of some mice. It appears probable that these lymphomas derived from the vertebral marrow, which was assumed by WATANABE (1958) to be the site of predilection for the development of strontium-induced leukaemias. The simultaneous occurrence of thymic lymphoma and of lymphoma deriving from the bone marrow of the vertebral column may indicate primary lymphomas both in thymus and bone marrow. This would in such case explain the doubling of the incidence of non-thymic lymphoma found after thymectomy of animals receiving the combined treatment (from 13 to 28 per cent). ITO et coll. (1969) also found that thymectomy appeared to favour the occurrence of strontium-induced non-thymic leukaemia.

There was no significant difference in mean latency time between thymic lymphoma and non-thymic lymphoma, which is in agreement with an earlier investigation on strontium-induced lymphomas (NILSSON 1971).

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SUMMARY

The effect of fractionated external whole body irradiation has been compared with the combined effect of such irradiation and of radiation from ^{90}Sr in respect of changes in the haematopoietic tissue and the development of lymphoma in mice. The investigation has

shown that the regeneration seen in haematopoietic tissues after roentgen irradiation is delayed if the external irradiation is supplemented by ^{90}Sr treatment. The delayed bone marrow regeneration leads, inter alia, to incomplete regeneration and increased incidence of lymphomas in the thymus. Strontium-induced non-thymic lymphomas increase in incidence if ^{90}Sr treatment is supplemented by small doses of external irradiation.

ZUSAMMENFASSUNG

Der Effekt fraktionierter externer Ganzkörperbestrahlung wurde mit dem kombinierten Effekt solcher Bestrahlung und der Bestrahlung durch ^{90}Sr hinsichtlich der Änderungen des haematopoietischen Gewebes und der Entwicklung von Lymphomen bei der Maus untersucht. Die Untersuchung zeigt, dass die Regeneration in den hämatopoietischen Geweben nach Röntgenbestrahlung verzögert ist, wenn die Externbestrahlung durch ^{90}Sr Behandlung ergänzt wird. Die verzögerte Knochenmarksregeneration führt unter anderem zu einer unvollständigen Regeneration und zu einem erhöhten Vorkommen von Lymphomen im Thymus. Strontium induzierte nicht-Thymus Lymphome treten gehäuft auf, wenn die ^{90}Sr Behandlung durch kleine Dosen externer Bestrahlung ergänzt wird.

RÉSUMÉ

L'auteur a comparé l'effet de l'irradiation corporelle totale externe fractionnée avec les effets associés de cette irradiation et du rayonnement du ^{90}Sr en ce qui concerne les modifications du tissu hématopoïétique et le développement des lymphomes chez des souris. Ce travail a montré que la régénération constatée dans les tissus hématopoïétiques après irradiation roentgen est retardée si l'irradiation externe est complétée par un traitement au ^{90}Sr. Le retard de la régénération de la moelle osseuse conduit, entre autres choses, à une régénération imcomplète et à une augmentation de la fréquence des lymphomes dans le thymus. La fréquence des lymphomes extrathymiques induits par le strontium augemente si le traitement par le ^{90}Sr est complété par de petites doses d'irradiation externe.

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