Effects of Radiation on The Capacity of The Stem Cell Compartment to Differentiate into Granulocytic and Erythrocytic Progeny

by Samuel Hellman, Helen E. Grate and John T. Chaffey

A VARIETY OF METHODS have been used to investigate the properties of the stem cell compartment. The spleen colony method introduced by Till and McCulloch measures the production of hematopoietic colonies after injection of syngeneic bone marrow into irradiated recipient mice. These colonies appear to be the progeny of single cells which are able to differentiate to form either granulocytic or erythrocytic progeny. Under most circumstances, the system is more a measure of erythrocyte production since the surface colonies in the spleen are predominantly concerned with erythropoiesis. Other technics which measure proliferation of hematopoietic cells within the spleens of animals recovering from whole body irradiation utilize spleen weight, incorporation of IUDR into the DNA of newly-formed cells, or incorporation of $^{59}$Fe into maturing erythrocytic cells.

A second type of assay system (repopulating ability) measures the ability of transplanted progenitor cells to form specific mature progeny. Irradiated recipient animals having received syngeneic bone marrow earlier will incorporate $^{59}$Fe into newly-formed erythrocytes. If one waits a sufficient period of time for proliferation and differentiation of the injected bone marrow progenitor cells before injecting the radioactive iron, then the incorporation of $^{59}$Fe is proportional to the number of bone marrow cells injected, and can be used to assay such marrow. Hodgson compared irradiated with normal marrow and constructed a radiation survival curve. Using this as a model, we have described a similar system in which the granulocytic progeny of the injected marrow are measured. In this system, irradiated recipient mice are given syngeneic bone marrow, a period of time is allowed for this marrow to proliferate and differentiate, and then bacterial endotoxin is injected. The peripheral white blood cell response to bacterial endotoxin has...
been shown to be a measure of the marrow granulocyte reserve.\textsuperscript{16} We have shown that the response to endotoxin is proportional to the bone marrow cells injected earlier and this can be used to assay the bone marrow progenitor compartment.\textsuperscript{9}

In this study, the response to radiation of murine bone marrow, as measured by these three assay systems, is investigated and compared.

**Materials and Methods**

Animals used in all experiments were male C3H/HEJ mice 8–12 weeks old.\textsuperscript{*} X-irradiation factors were 250 kv, 15 ma. HVL 1.5 mm of copper, FSD of 50 cm. The dose rate for whole animal radiation was approximately 114 R per minute. Dose measurements were made in a mouse “phantom” using a Baldwin-Farmer dosimeter whose calibration was confirmed by the National Bureau of Standards. Before and after irradiation, animals were placed in cages of 8 animals and supplied with food and water ad libitum. When bone marrow was irradiated in vitro, the cells were irradiated at 37 cm. from the anode in Tyrode solution, at room temperature while vigorously bubbled with oxygen.

Bone marrow cell suspensions were prepared by flushing the medullary cavity of the tibia and femur with cold sterile Tyrode solution. Cell suspensions were kept on ice until used, and were injected intravenously into the lateral tail vein not longer than 90 minutes following removal. A sufficient volume of solution was used so that the injected bolus varied between 0.05 and 0.4 ml. Cell counts were made using a hemocytometer. Donor marrow was taken immediately or at scheduled times following irradiation. All donor marrow was pooled from both hind limbs of at least two donors.

**Assay of Erythrocytic Repopulating Ability of the Transplanted Bone Marrow**

Recipient animals were exposed to 700 R. whole body irradiation and within two hours injected with graded doses of syngeneic normal bone marrow suspended in Tyrode solution. Similar litter mate animals were injected with irradiated bone marrow. This marrow was taken either from donor mice immediately or at indicated times after irradiation with the appropriate dose, or from normal mice and irradiated in vitro as described above. Seven or nine days were allowed for the cells to proliferate. The animals then received 0.5 μc. of \textsuperscript{59}Fe as ferrous citrate. Two days later, a cardiac puncture was made and 0.5 ml. of blood removed and counted in a well scintillation counter. The per cent of \textsuperscript{59}Fe incorporation was then calculated assuming a blood volume of 0.86 cc. per 10 Gm. of body weight. The per cent of \textsuperscript{59}Fe incorporation was then plotted against the number of bone marrow cells injected. This can be used to estimate the number of viable cells necessary to produce the same \textsuperscript{59}Fe uptake as that produced by a larger number of irradiated cells. From this a survival fraction can be determined. Using this analysis as described by Hodgson\textsuperscript{6} and Blackett,\textsuperscript{8} a survival fraction was determined. Each determination used a test group of six to eight mice injected with irradiated marrow and three groups of six mice, each group receiving a different dose of normal bone marrow. An additional group of six mice served as an uninjected control.

**Assay of the Granulocytic Repopulating Ability of the Transplanted Bone Marrow**

This system has been described in detail previously.\textsuperscript{9} Recipient animals were exposed to 700 R. whole body radiation and within two hours injected intravenously with graded doses of unirradiated syngeneic bone marrow. Similar litter mate animals were injected with irradiated marrow. This marrow was taken from donor mice either immediately or at indicated times after irradiation in donor animals or was taken from normal mice and irradiated in vitro as described above. Seven, nine, or eleven days were allowed

\* Supplied by Jackson Laboratories, Bar Harbor, Maine.
for the bone marrow cells to proliferate and then the animals were injected intravenously
with $10^{-2}$ gamma of Pyrexal, a bacterial endotoxin isolated from Salmonella abortus-
equi.* The white blood cell count of each animal was measured immediately before
and at two, four, and six hours following the injection using a Coulter Electronic Counter
model B. The maximum white blood cell responses in the animals were then grouped
and plotted against the number of cells injected earlier. Compared to this was the white
blood cell response in that group of animals injected with irradiated bone marrow. From
this, one can estimate the number of viable cells necessary to produce the same white
blood cell count that a larger number of irradiated cells produced, and a survival
fraction can be determined. White blood cell counts were used since the response to
endotoxin in this method has been shown to be a granulocyte response. This obviates
the need for differential counts. Each determination of survival fraction used a test group
of six to eight mice injected with irradiated marrow and three groups of six mice, each
group receiving a different dose of normal bone
marrow. An additional group of six
mice served as an uninjected control.

Spleen Colony Method

Recipient mice exposed to 865 R. whole body irradiation and within two hours
injected with normal syngeneic bone marrow. Similar litter mate recipients received bone
marrow intravenously from donor animals previously irradiated. Nine days later, the
surviving animals were sacrificed, the spleens removed and placed in Bouin’s solution.
Twenty-four hours later, macroscopically-visible colonies were counted. The number of
colony-forming units was calculated and a survival fraction determined. Each determina-
tion was based on counting at least ten spleens in each normal and irradiated bone
marrow group. Eight hundred sixty-five R was necessary to reduce control colony count to
less than one colony per spleen in irradiated animals not receiving bone marrow. Such a
control group was scored with each experiment and the colony number subtracted from
the experimental groups.

RESULTS

Stem Cell Compartment as Measured by the Granulocytic Repopulating
Ability

Previous experiments had used a seven-day period between injection of
unirradiated bone marrow and subsequent stimulation by endotoxin as a
satisfactory time for proliferation and differentiation. Using this time
interval, the radiation survival was determined (Fig. 1). Characteristically,
radiation survival curves drawn in this fashion have an initial shoulder and
then a straight portion. Two common parameters are used to describe such
curves: first, the $D_0$, which is the dose needed to reduce the population to
37 per cent as measured on the straight portion of the survival curve; and
second, the value of the ordinate when the straight portion of the curve is
extrapolated back to zero dose. A straight line can connect the points;
however, it does not conform to the typical radiation survival curve. The
$D_0$ is quite large (285 R.) and the extrapolation number considerably less
than one (0.66).

Next investigated was the effect of increasing the time allowed for pro-
liferation and differentiation. Figure 1 shows a more conventional radiation
survival curve obtained when nine days are allowed between injection of
the cells and measurement of the response to endotoxin. There is some scatter
in the points, but a $D_0$ of 108 R. and an extrapolation number of 1 can be

*Originally prepared by the Dorsey Laboratories, Lincoln, Nebraska.
Fig. 1.—Survival curve of bone marrow irradiated in vivo as assayed by the white blood cell response to endotoxin in recipient animals. Lines fitted by regression analysis using the method of least squares. Seven day interval resulted in $D_0 = 285 \pm 22$ R and an extrapolation number of 0.66. The nine day interval resulted in a $D_0$ of $108 \pm 14$ R with an extrapolation number of 1. All points are indicated with their standard errors.

calculated. To determine whether additional time for proliferation would show progressive decrease in $D_0$, 11 days were allowed between injection of bone marrow and endotoxin. No increase in radiation sensitivity was noted (Fig. 2).

Stem Cell Compartment as Measured by Erythrocytic Repopulating Ability

A survival curve using the $^{59}$Fe assay system is shown in Figure 3. A conventional radiation survival curve is seen with a $D_0$ of 77 r. and an extrapolation number of 1. Because of the results using the endotoxin assay system, an increased time for proliferation was investigated. Nine days were allowed between bone marrow and injection of $^{59}$Fe. No increase in sensitivity was noted (Fig. 3).

It is important to note that the stem cell pool shows different survival characteristics when assessed by the ability to form erythrocytes as compared to that observed by the capacity for granulocyte production. This is shown in Table 1. The calculation of $D_0$ and extrapolation number is
limited in both methods because of the limited range of doses studied. This is due to the large number of cells necessary for injection when a large amount of radiation is given. However, a significant difference in sensitivity is seen when the two most commonly studied doses, 200 R. and 300 R., are evaluated. Also included in Table 1 are the survivals at these doses using the spleen colony method. The results of the endotoxin and spleen colony assay methods are similar, but the stem cell pool is significantly more sensitive when measured by its ability to produce erythrocytic progeny.

It is of interest to determine whether this difference in radiation sensitivity as measured by the ability to produce these two differentiated progeny is present when the bone marrow is irradiated in vitro as well as in vivo. The results of such experiments can be seen in Table 2. The in vitro results are similar to those in vivo. The difference in sensitivity of the stem cell pool as measured by the two assay systems is still evident. The erythropoietic
Fig. 3.—Survival curve of bone marrow irradiated in vivo as assayed by the incorporation of $^{59}$Fe into newly-formed erythrocytes in recipient animals. Both seven and nine day intervals were allowed between bone marrow transplantation and $^{59}$Fe injection. The $D_0$ calculated from the seven day data equals 77 ($\pm$ 9) R and the extrapolation number 1. All points are indicated with their standard errors.

assay indicates the stem cell pool to be significantly more sensitive and serves to confirm the in vivo results.

Recovery from 200 R.

The results of assaying the erythropoietic repopulating ability of bone marrow taken from animals immediately and at varying days after 200 R. is shown in Figure 4. The initial survival fraction is reduced to 0.087 ($\pm$ 0.013). Following this, there is a prompt postirradiation dip reaching a nadir between days one to four, followed by a subsequent rise. The experiment is continued to day 25 when the repopulating ability has not yet returned to control levels although it appears to have a progressively decreasing recovery rate. The postirradiation dip shows at least a fivefold reduction from the initial response to irradiation.
Table 1.—Sensitivity of Bone Marrow Stem Cells Irradiated In Vivo as Measured by Three Assay Methods

<table>
<thead>
<tr>
<th>Dose</th>
<th>Assay Technic</th>
<th>Survival Fraction</th>
<th>Mean</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mean</strong></td>
</tr>
<tr>
<td>200 R.</td>
<td>$^{59}$Fe (7 day)</td>
<td>0.12(±.02), 0.08(±.02), 0.09(±.02), 0.058(±.009)</td>
<td><strong>0.087(±.013)</strong>*</td>
</tr>
<tr>
<td></td>
<td>Endotoxin (9 day)</td>
<td>0.20(±.07), 0.27(±.04), 0.09(±.02), 0.26(±.05), 0.13(±.01), 0.14(±.04)</td>
<td><strong>0.18(±.03)</strong>*</td>
</tr>
<tr>
<td></td>
<td>Spleen Colony</td>
<td>0.26(±.04), 0.15(±.06), 0.13(±.06)</td>
<td><strong>0.18(±.04)</strong></td>
</tr>
<tr>
<td>300 R.</td>
<td>$^{59}$Fe (7 day)</td>
<td>0.020(±.004), 0.041(±.008), 0.023(±.005)</td>
<td><strong>0.028(±.007)</strong>†</td>
</tr>
<tr>
<td></td>
<td>Endotoxin (9 day)</td>
<td>0.11(±.03), 0.048(±.028), 0.052(±.008)</td>
<td><strong>0.070(±.020)</strong>†</td>
</tr>
<tr>
<td></td>
<td>Spleen Colony</td>
<td>0.087(±.020), 0.11(±.03)</td>
<td><strong>0.099(±.012)</strong></td>
</tr>
</tbody>
</table>

* Difference significant with P = < .05.
† Difference suggestive with P = < .15

Considered together using the formula $X^2 = -\frac{1}{2} \log_e P$, P = .03

Numbers in parentheses are the standard errors.

Table 2.—Radiation Sensitivity of Bone Marrow Stem Cells Irradiated In Vitro

<table>
<thead>
<tr>
<th>Dose</th>
<th>Assay Technic</th>
<th>Survival Fraction</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Mean</strong></td>
</tr>
<tr>
<td>200 r.</td>
<td>$^{59}$Fe (7 day)</td>
<td>0.066(±.004), 0.064(±.011), 0.064(±.018)</td>
<td><strong>0.081(±.014)</strong>†</td>
</tr>
<tr>
<td></td>
<td>Endotoxin (9 day)</td>
<td>0.18(±.09), 0.28(±.04), 0.16(±.04), 0.16(±.05)</td>
<td><strong>0.20(±.029)</strong>†</td>
</tr>
<tr>
<td></td>
<td>Spleen Colony</td>
<td>0.033(±.005), 0.039(±.009)</td>
<td><strong>0.036†</strong></td>
</tr>
<tr>
<td>300 r.</td>
<td>$^{59}$Fe (7 day)</td>
<td>0.033(±.005)</td>
<td><strong>0.036†</strong></td>
</tr>
<tr>
<td></td>
<td>Endotoxin (9 day)</td>
<td>0.058(±.016), 0.078(±.025)</td>
<td><strong>0.068</strong></td>
</tr>
<tr>
<td></td>
<td>Spleen Colony</td>
<td>0.078(±.025)</td>
<td><strong>0.070(±.020)</strong></td>
</tr>
</tbody>
</table>

* Difference significant P = < .01
† If both in vivo and in vitro results are considered together, the differences between the assay techniques are significant with P = < .01 (200 R)
P = < .02 (300 R)

Numbers in parentheses are the standard errors.

Bone marrow taken from animals immediately and at varying times after 200 R., is assayed for granulocytic repopulating ability using a seven-day proliferative period following transplantation (Fig. 5). The initial survival fraction is 0.33 (±.02). Following this, there is a postirradiation dip reaching a nadir on day eight followed by recovery with some overshoot. The difference in the assayed results using periods of seven or nine days after transplanta-
RECOVERY OF GRANULOCYTIC PROGENY

Fig. 4.—Fraction of cells surviving 200 R. as measured by the erythrocytic repopulating ability, of donor cells removed at various times after radiation. The donor bone marrow was allowed to proliferate for seven days before 59Fe injection. All points are listed with their standard errors.

tion to measure the granulopoietic system prompted repeating these experiments using a proliferative period nine days following transplantation before assay. This is shown in Figure 6. The initial survival fraction is (0.18 ± 0.03), followed by a similar postirradiation dip. This reaches a nadir on day eight as did the results using the seven-day proliferative period. This dip is as low as .05 and represents an approximate fourfold reduction from the immediate postirradiation response. Following this, there is a gradual recovery of the granulocyte repopulating ability. The last day studied was day 21, and, at this time, normal levels had not been reached although the system appeared to demonstrate a decreasing recovery rate. The results of the two proliferation periods using the granulopoietic repopulation assay are quantitatively different but are qualitatively similar in that the nadir and subsequent rise occur with the same temporal relations (Fig. 7).

Figure 8 compares the temporal changes in erythropoietic repopulation
Fig. 5.—Fraction of cells surviving 200 R. as measured by the granulocytic repopulating ability of donor cells removed at various times after radiation. The donor bone marrow was allowed to proliferate seven days before endotoxin administration. All points are listed with their standard errors.

Assay to that of the granulopoietic. Initially, following irradiation, the survival fractions are significantly different. Following this, the erythropoietic ability of the stem cell pool falls to extremely low levels and then demonstrates rapid recovery. The granulopoietic repopulating ability continues to fall and does not begin to recover until after day eight. After day eleven, both functions increase but do not reach normal levels during the period studied.

**Discussion**

We interpret the difference in survival of the stem cell pool as measured by its ability to produce granulocytic progeny when measured seven days as compared to nine days after irradiation to indicate that the seven-day time period measures not only the continued proliferative ability of the stem cell pool, but also cells requiring only a limited number of divisions before producing nondividing granulocytic precursors. Since a limited number of divisions may follow radiation in clones not destined to ultimately proliferate,19,20 it is quite conceivable that the shorter period of time will give a
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Fig. 6.—Fraction of cells surviving 200 R. as measured by the granulocytic repopulating ability of donor cells removed at various times after radiation. The bone marrow was allowed to proliferate nine days before endotoxin administration. All points are listed with their standard errors.

Falsely high estimate of the number of cells surviving radiation. This could be considered analogous to the counting of these “abortive” as well as “true” colonies as described by Puck and Marcus. It appears from the data that nine days are sufficient when assaying by the production of erythrocytic progeny.

This study is related to the question of the potential of the stem cell to produce more than one type of differentiated progeny. There now appears to be good evidence for the presence of a common hematopoietic stem cell. Wu et al. have demonstrated that spleen colonies derived from a single progenitor cell can produce differentiated progeny of both granulocytic and erythrocytic type. Harris et al. found that after large acute hemorrhage, the number of granulocytic precursors in the guinea pig bone marrow is reduced. We have shown that increased demand for red blood cell production in the recipient either by bleeding or erythropoietin decreases the ability of transplanted syngeneic bone marrow to produce granulocytic progeny. Mice, pre-irradiated with low doses (150–160 R.) six to seven days before 700 R. and injection of bone marrow, are better recipients when determined by their ability to produce erythrocytic progeny and are concomitantly...
poorer recipients as determined by their ability to produce granulocytic progeny. All these data support the notion of a common hematopoietic stem cell pool on which competing proliferative demands can be made. In order to understand the effects of radiation on the hematopoietic stem cell pool, therefore, one must study not only the ability of the stem cell to replicate but the ability to produce specific differentiated forms as well.

The stem cell appears more sensitive when measured by erythrocytic progeny than by granulocytic progeny, the D₀ for erythropoietic and granulopoietic assays being 77 R. and 108 R. respectively. This is consistent with the results of Hodgson showing D₀ of 71 R. measuring erythrocytic progeny. In order to reconcile these apparent differences in survival of the stem cell when measured by these assay systems, two possible hypotheses can be entertained. The first is that there are, two different stem cells, and thus, these two systems measure entirely different pools. The evidence previously discussed in favor of a common stem cell pool would seem to argue against this. The second, and, to us, more appealing explanation is that there is a common stem cell pool but that radiation affects the differentiation pattern of the stem cells. Consistent with this is the data demonstrating a reduction in the ratio of erythrocytic to granulocytic spleen colonies derived

Fig. 7.—Comparison of curves of stem cell recovery following 200 R. measured by granulocytic repopulating ability. Time between transplantation and assay was seven (from Fig. 5) or nine (from Fig. 6) days.
Fig. 8.—Comparison of stem cell recovery following 200 R. measured by granulocytic repopulating assay (from Fig. 6) and erythrocytic repopulating assay (from Fig. 4).

Recovery from 200 R. is quite different as measured by the two repopulation assays. In both curves radiated marrow is compared to normal marrow. No correction is made for any possible change in total marrow cellularity. However, since any such change will affect both curves similarly, the described relationships remain valid. It appears that initially granulopoiesis is spared. This is demonstrated by the initial difference in survival fraction and early fall in erythropoietic repopulating ability. Following this, there is preferential recovery of erythropoietic repopulating ability from days four to eight while granulopoietic repopulating ability is still diminishing. After day eight, both show recovery. This is related to the phenomenon of “pre-irradiation” in which mice recovering from low doses of irradiation have an increased capacity to support erythropoietic proliferation of transplanted bone marrow. Concomitant with this increase is a decrease in the ability of such
recipients to support granulopoiesis of transplanted marrow. Blackett and co-workers* have preliminary data indicating that such an effect of pre-irradiation may start as early as day three and reach a maximum in seven to ten days, gradually diminishing thereafter. Such a time course would be consistent with the data reported here in these experiments. This study demonstrates a rapid increase in erythropoietic recovery while granulopoiesis is still decreasing or only slowly rising. Both the pre-irradiation experiments and the results reported here indicate that beginning several days after irradiation, stem cell differentiation is preferentially directed toward erythropoiesis as opposed to granulopoiesis. This is the reverse of what appears to be happening immediately postirradiation when granulopoiesis is conserved at the expense of erythropoiesis.

These effects on the direction of stem cell differentiation are dependent upon the milieu in which the stem cell finds itself. This is demonstrated by the described effects of “pre-irradiation” of the recipient on transplanted bone marrow. In such experiments, stem cells removed from unirradiated recipients will be preferentially directed toward erythropoiesis when placed into recipients recovering from irradiation. This is not the case when such cells are placed into recipients not pre-irradiated. The direction of normal or irradiated stem cell differentiation is influenced by the in vivo environment. If the cells are left in the donor for periods of time before transplantation, this environment affects the proliferation and differentiation. Six days after radiation, transfer of cells to preirradiated recipients has no effect, presumably because during these six days, differentiation pressures have been determined by the donor animal itself recovering from radiation. These pre-irradiation experiments attempt to discern the effects of radiation on the ability of the mouse to produce erythrocytes and granulocytes. They indicate that the changes in direction of differentiation in this experiment following 200 r. are mediated not by the cell but by the host animal.

A number of other experiments demonstrating the temporal changes in the stem cell compartment following irradiation have been reported. None of these enable comparison of the recovery of the stem cell compartment as measured by the ability to produce these two types of progeny. All those requiring transplantation of a small number of irradiated cells into irradiated recipients demonstrate a “postirradiation dip,” i.e., progressive decrease in survival for a period of time following transplantation. The reason for this dip is unknown and a variety of mechanisms have been suggested. To us, the most appealing explanation is that the dip is due to the extent and direction of differentiation which may temporarily exceed stem cell capacity for self replication and result in the depletion of the stem cell pool. While discussions of these mechanisms are conjectural, some final conclusions can be drawn from these studies.

The stem cell pool, as measured by the ability to produce erythrocytic progeny, is initially more sensitive to radiation than when measured by its ability to produce granulocytic progeny. This is true when the cells are

*Blackett, N. M. Personal communication.
irradiated in vivo or in vitro. Following this initial event, the erythropoietic repopulating ability falls more rapidly and begins to recover earlier than the granulopoietic repopulating ability. Since a number of experiments indicate that both these progeny have a common stem cell on which competing proliferative demands can be made, these results can be interpreted as indicating that radiation affects not only survival but the direction and extent of differentiation as well. It appears that an initial effect of radiation is to decrease the erythrocytic differentiation of the stem cell pool, presumably conserving granulopoiesis; the reverse situation exists in the recuperative period. These effects appear to be due to the host milieu and not to the direct effect of radiation on the stem cell.

Summary

Different methods have been used to measure the survival following radiation of the hematopoietic stem cell pool. Two of these systems measure the stem cell pool by its ability to proliferate and differentiate into mature progeny. In both methods, irradiated recipient mice receive syngeneic bone marrow. A period of time is allowed for the transplanted progenitor cells to divide and differentiate, and then the progeny produced are assayed. Ability to form red blood cells is assessed by the amount of radioactive iron incorporated into newly-formed erythrocytes. Capacity for granulocyte formation is measured by peripheral white blood cell counts following endotoxin stimulation. This latter is a granulocyte response and has been shown to be a measure of the marrow granulocyte reserve. The pool as measured by its ability to produce erythrocytic progeny appears to be more sensitive initially than as measured by its ability to produce granulocytic progeny. Erythropoietic repopulating ability begins recovery more promptly than the granulopoietic. These effects appear to be due to the host milieu rather than any direct effect of radiation on the stem cells, resulting in initial conservation of granulopoiesis relative to erythropoiesis with subsequent compensatory recovery of erythropoiesis. Because of recent evidence suggesting a common stem cell, these results are interpreted as consistent with the notion that radiation affects not only stem cell proliferation, but also the direction and extent of differentiation.

SUMMARIO IN INTERLINGUA

Varie methodos esseva usate pro measurar le superviventia postradiatori del pool hematopoietic de cellulas primordial. Duo de iste systemas mesura le pool de cellulas primordial a base de su capacitate de proliferar e de differentiar se in descendentes matur. In ambe iste, methodos, le muses recipiente le radiation etiam recipe syngenic medulla ossee. On lassa passar un certe periodo de tempore pro que le transplantate cellulas progenitori pote divider e differentiar se, e postea le progenie producite per illos es evaluata. Le capacitate de formar erythrocytos es evaluata a base del quantitate de ferro radioactive incorporata in novemente formate erythrocytos. Le capacitate de formar granulocytes es mesurata per le numeracion de leucocytes peripheric post stimulation con endotoxina. Iste ultimes es un responsa granulocytic, e il ha esite mostra que illo representa un mesura del reservas granulocytic in le medulla. Le mesuration del pool a base de su capacitate de producer progenie erythrocytic pare esser plus sensibile que su mesuration a base de su capacitate de producer progenie granulocytic. Le capacitate de effectuar un repopulation erythro-
RADIATION AND THE STEM CELL COMPARTMENT

poietic se restabl plus promptemente que le capacit de effectuar le repopulation granulopoietic. Iste effectos pare esser causate per le milieu del hospit e toso que perulle efecto directe del radiation super le cellulas primordial, resultante in conservation initial del granulopoiese relative al erythropoiese con le subsequente restablimento compensatori del erythropoiese. A causa de recente evidencia suggesto un commun cellula primordial, iste resultatos es interpretate como compatible con le idea que radiation affice non solo le proliferation del cellulas primordial sed etiam le direction e le mesura del differentiation.

REFERENCES


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