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PATHOGENESIS AND REGENERATION OF RADIATION INDUCED BONE MARROW
INJURY, AND THERAPEUTIC IMPLICATIONS.* /

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INTRODUCTION:

It has been known for decades that the hemopoietic tissues are sensitive to ionizing radiation. This knowledge has been applied in radiotherapy since the beginning of this century in the treatment of leukemia and polycythemia vera. Recently more consideration has been given to the use of total body irradiation in the treatment of generalized malignant processes in part because it has been assumed that better therapeutic means are now available for the treatment of bone marrow depression which inevitably follows large doses of radiation to the whole body.

Total body irradiation of man became of clinical importance because of the possibility of nuclear warfare and of radiation accidents. Radiation injury is one of the best studied hazards in modern life. However, many aspects of the pathogenesis and factors involved in the recovery from radiation injury of the blood cell forming organs remain unclear. The purpose of this paper is to review some aspects of experimental and clinical research performed in the course of investigation on the pathogenesis and recovery of bone marrow injury caused by total body irradiation. Since the hemopoietic response may be altered by neoplastic diseases, data derived from individuals, presumably healthy at the time of irradiation, are more suitable for such a study than are data from total body irradiation of patients with a neoplastic disease.

1. Blood cell changes in man after radiation injury.

The blood cell changes of 5 persons, accidentally exposed to mixed neutron-gamma radiation in Oak Ridge (Fig.1) appear to be characteristic for man for the low to mid-lethal dose range. These data and detailed information concerning the accident have been reported extensively (1). The estimated radiation doses to the individuals ranged from 236 to 365 rad. The platelets

oscillated with a downward trend for the first 10 days and thereafter gradually declined to minimum between 25 and 30 days. Recovery of the platelet count commenced thereafter.

The leukocyte count showed initial fluctuations during the first few days after irradiation. Then a decline was apparent with a first minimum at 9 days which was followed by a transient rise between the 10th and 20th day. A final minimum occurred between the 25th and 30th day before a sustained recovery of the leukocyte count became recognizable.

The reticulocytes were low in the initial phase and showed evidence of a slight transient increase between day 10 and 20 and finally a sustained increase overshooting the normal level around the 35th day. Due to the long lifespan of the red cells and in the absence of gross blood loss in the exposed individuals (two of them showed petechiae and oozing of the gums at the time of most severe thrombocytopenia), the hematocrit and hemoglobin concentration decreased only slightly during the second month after exposure. Thus, anemia does not appear to be a significant problem after these doses.

The lymphocytes dropped below normal limits within a few days and remained at this level without much fluctuation until they gradually returned towards normal beyond the 30th day. Of particular interest were the changes in the number of mononuclear blood cells capable of incorporating tritiated thymidine in vitro (2). As has been reported (3,4), the number of these mononuclear cells labeled in vitro drops to zero shortly after exposure. There is a transient rise above normal levels around the 12th day. Normal values were again found around the 28th day. A second transient rise to values above normal was seen around the 40th day. Normal values were found 4.5 months after the accident. The fate and function of these cells remain unknown. The incorporation of tritiated thymidine indicates that these cells

are synthesizing DNA and thus are destined in all probability to undergo further mitosis. It is, however, of interest, that their numerical changes parallel those of the neutrophils and reticulocytes rather than the lymphocytes.

In March 1960, a radiation accident occurred in Lockport, N. Y. in which nine civilian technicians were exposed to x-radiation while attempting to tune a newly installed malfunctioning klystron tube. This accident and the clinical findings have been reported previously(5). There is a large uncertainty in estimates of the x-ray dose received by the individuals. Four of them developed clinical signs and symptoms of radiation injury. Their blood cell changes are shown in Figure 2. All of them received a higher dose of radiation to the head than to the trunk. In the two most heavily exposed individuals the head received at least 1000 r, the trunk about 300 r of x-ray. The radiation exposure doses of the two other individuals were about 400 r to the head and 180-320 r to the trunk. It is apparent (Fig. 2) that there is considerable variation in the blood cell changes from person-to-person as might be expected from such inhomogeneous total body irradiation. However, it is still of interest to compare the trends of these curves with those obtained in the 1958 Oak Ridge accident.

The platelets remained within about normal limits for 10 days. Thereafter, a marked decrease occurred particularly in patient A and B who received the heaviest exposure. A minimum was reached in A, D and C around the 20th day, while the count continued to fall in B until about the 28th day. In patient A, C and D, recovery occurred and approximately normal levels were reached by the 32nd day. In B, the platelet count remained low without evidence of marked recovery throughout the time of observation. The leukocyte

count showed a marked initial fluctuation, mostly due to changes in the neutrophil count. The lymphocytes dropped below normal limits initially and remained almost constant for the next 3 weeks at least. Between the 4th and the 10th day the slope of decrease in the total white count appeared to be similar in the Lockport and the Oak Ridge patients. Thereafter there was a transient rise in the white counts in some patients. However, in the most heavily exposed individuals A and B, the counts declined again, while in C the count remained at the lower limit of normal. In D, the total white count remained in the normal range. The lymphocyte count reflected the severity of the radiation injury. The counts of A and B remained below normal limits throughout the first 52 days. Those of C were at the low normal range and those of D returned to normal around the 25th day. However, it is apparent from the comparison of the Oak Ridge and the Lockport data and the clinical course, that lymphocyte counts may not give adequate information as to the probable outcome of the other blood cell changes or the overall prognosis.

The third radiation accident in which the blood cell changes will be considered occurred in Vinca, Yugoslavia in October 1958. Details of the accident and the hematological data have been reported in detail by Drs. Jarret and Mathè (6,7). For comparative purposes, the reported data are plotted on the same scale as the Oak Ridge data (Fig. 3). The fourth accident, due to exposure to fallout radiation to which reference is made, occurred on March 11, 1954 in the Marshall Islands. Details of the accident have been reviewed in detail (8).

In Figure 3a, b and c, the platelet counts, the leukocyte counts and the lymphocyte counts of the Rongelap, the Oak Ridge and the Vinca accident are plotted using the same scale.* In Figure 3d, the reticulocyte counts of

* In the figures, the horizontal lines give approximate upper and lower limits of the various blood cell types that apply in usual American and European hematology. The lines in the Rongelap data do not reflect the values for normal comparison individuals of the Island populations, which differ considerably from the usual "western" normal values, and the blood cell changes are much more pronounced than one may conclude from the curves as discussed in the text.

the Oak Ridge and the Vinca casualties are compared. Detailed analyses of these data have been given previously (4,9). For the discussion of this paper, only a few points will be emphasized. The comparison of the platelet counts of all 4 accidents indicates, that recovery occurred in all those patients in whom the initial drop did not become severe before the 10th day after exposure. The characteristic platelet curve in the more homogeneously total body irradiated individuals shows a minimum between the 25th and 30th day. The three individuals of the Lockport accident received markedly inhomogeneous whole body radiation. In individuals A, C, and D recovery commenced about 10 days earlier than in the others with non-lethal but with relatively homogeneous total body irradiation. One of the Vinca casualties died on the 30th day. His platelet count decreased much more rapidly attaining minimum levels between the 10th and 15th day suggesting a more severe radiation injury. Since platelets in human beings have a lifespan of about 10 days (10,11), such a rapid disappearance probably indicates complete suppression of platelet formation. In the other curves in which the decrease commences only after about ten days, the slope would indicate some further platelet production and maturation and is therefore termed "delayed". The "delayed decrease" suggests that the exposure has been below the 100% lethal dose and thus there is a statistical chance of survival.

The leukocyte curves (Fig. 2, 3b), particularly those of the Oak Ridge and the Lockport accident, and the reticulocyte curve (3c) may be considered together. Of interest is the initial fluctuating leukocytosis, seen in the Oak Ridge casualties in particular, in which early determinations were performed. Such an initial fluctuation with a leukocytosis has been documented

also in animal experiments and was considered to represent a release of the marrow granulocytic pool (12,13). Both the leukocyte and reticulocyte counts showed some evidence of a transient improvement of counts between days 10 and 20 in the Oak Ridge casualties. This was less obvious in the leukocytic counts of the Vinca casualties, which were not taken as frequently but more obvious in the reticulocyte counts of these individuals. In 3 of the Lockport casualties, it appeared as if leukocyte regeneration commenced during this period of "transient" recovery in the more uniform and heavily exposed individuals. Reviewing the leukocyte curves as a whole, it appears that the "transient" recovery of leukocytes and reticulocytes between day 10 and 15 can be considered in parallel to the "delayed" platelet decrease as evidence that the bone marrow may recover.

In the blood smears of the Oak Ridge casualties unusually large granulocytes were seen around the 8th to 10th day. This suggests that some abnormal new blood cell formation is occurring. Further evidence of blood cell formation during this phase is the transient rise in numbers of mononuclear cells capable of labeling with tritiated thymidine, around day 12. In animal experiments, a transient granulocyte rise ("abortive rise") has been observed repeatedly (13,14) characterized in part by unusually large cells. This rise occurs around the 7th day in the rat and can be correlated with foci of "abortive" myelocytic regeneration on the 4th and 5th day in an otherwise markedly depleted marrow. However, this marrow may still be capable of a final spontaneous regeneration, if the sequelae of pancytopenia ("bleeding and infection") can be controlled (13,15).

Since lymphocyte counts have been used to determine the extent of acute radiation damage of the blood cell forming tissue, it is of interest to

compare the lymphocyte data of the four accidents (Fig. 2,3c). There was an approximately 50% decrease in the lymphocyte count in the Rongelap data (mean of 49 adults, exposed to approximately 175 r total body irradiation compared to the unirradiated control group of Marshallese (normal mean in the control group was $4100/\text{mm}^3$). In the Oak Ridge accident, the lymphocyte count dropped below normal limits within a few days (except for some fluctuations). Except in one patient who showed a marked recovery in all cell-forming systems, the lymphocyte count remained subnormal until it eventually returned to normal limits around the 40th day. This type of slope is seen in only one of the Vinca casualties (B), who had the least exposure and did not receive a bone marrow transfusion. The counts of the other Vinca casualties were lower than those of the Oak Ridge casualties which indicates that they received an overall more "effective" dose than the upper limit of the Oak Ridge casualties. It remains unknown, whether the slope of the lymphocytic curve beyond about the 30th day, which remained below normal, was influenced by the marrow transfusions given between the 25th and 35th days (indicated by arrows and the initials). The limited value of the lymphocyte curve to predict the hematological outcome after radiation exposure in some instances can be derived from a comparison of the "Oak Ridge" and Vinca data ("whole body" exposure) with the Lockport (markedly non-homogeneous exposure) lymphocytic curve. These counts, particularly those of patient A and B, simulate closely those of the most heavily exposed Vinca casualties. However, patient A showed a marked, early recovery in the other blood cell systems while B remained subnormal but was able to overcome the radiation effects without specific treatment. Also, patient C, whose lymphocyte curve simulates that of patient B of the Vinca accident, showed a marked "early" platelet recovery and his leukocytes never dropped markedly below normal limits.

2. Hemopoietic activity of the bone marrow after radiation injury.

Three distinct phases may be observed:

- a. Initial destruction.
- b. Transient or "abortive" recovery.
- c. Effective regeneration.

Initial destruction was observed only in the Oak Ridge patients since early bone marrow studies were not performed on the Rongelap, Vinca, or Lockport patients. Aspirations were made at 12 and 36 hours after the accident in the Oak Ridge patients. At these times cytologic abnormalities were observed that are comparable to earlier more extensive observations made on animals (15,18). Various stages of karyorrhexis was observed in the erythrocytic series primarily in the basophilic normoblasts at the 12 hour interval. Karyorrhexis in animals is more marked at earlier time intervals and may have been underestimated in these patients. The second type of cytologic changes observed are so-called "mitotically connected" abnormalities. These are characterized by chromosomal fragments or free "chromosomes" in the cytoplasm of anaphase, telophase and interphase cells. Binucleated myelocytes and metamyelocytes are seen some of which have chromatin bridges. Lastly, some erythrocytic precursors possessed large nuclei approximating the basophilic normoblast and polychromatic cytoplasm. These cells are presumed to have been produced by the failure of nuclear division with continuation of cytoplasmic maturation. These abnormalities probably parallel a deficiency in production. The deficiency in production is certainly dependent upon the degree of cellular injury which is a function of the dose received. The phenomena observed will depend upon the radiation injury at the various stages of proliferation as illustrated in Fig. 4. Chromosomal fragments and free chromosomes in the cytoplasm of interphase cells

and cells in ana- or telophase were found. Other cells (myelocytes, meta-myelocytes) had two nuclei, some with and some without chromatin "bridges" between them. If the dose is high enough to block all or nearly all further proliferation and maturation, none or hardly any cells produced after radiation would be released into the circulation. The cells in the circulation would then disappear as a function of their life span. Pictures of radiation induced cytological abnormalities have been published recently for man (17) and for animals (15,18) and quantitative observations on the initial destruction phase have been reported (19,20).

Histologically, the initial phase of bone marrow destruction is characterized by a marked effect on the vascular integrity as well as on the cells themselves. It was shown in rats (13,15,21) and dogs (18) that the normally well outlined sinusoidal architecture of the marrow is disrupted within 24 hours, with extravasation of blood and finally frank hemorrhage. The change occurred earlier with higher doses. In the rat and dog, maximal destruction of the marrow with hemorrhage loss of architecture and marked cell depletion is seen by 3 to 4 days after doses in the mid-lethal range and higher. No initial systematic serial histological studies on human marrow after exposure to ionizing radiation have been performed. It is reasonable to assume that a similar breakdown in the sinusoidal architecture occurs in man as well. It has been pointed out that "bleeding" thus occurs in the bone marrow at a time when the platelet count is not low, and when there is no other evidence of extravasation of red cells in other organs (13,18). Regeneration of the marrow does not occur in areas of the marrow where the normal circulatory pattern has not been reestablished. It has been speculated that the extensive marrow hemorrhage following sinusoidal disintegration interferes with the regeneration and thus delays

recovery as compared to other tissues with comparable cell turnover rates (22)

The "transient" rise of various blood cells in the peripheral blood of radiation casualties must be interpreted in the light of events which are transpiring in the marrow. It has been reported (23) that the mitotic index in the Oak Ridge casualties reached a minimum after 4 days. A transient rise in the mitotic activity was found on day 8. Although the significance of changes in the mitotic index is extremely difficult to evaluate (24), it appears that this transient rise may reflect a phase of particular marrow activity of an "abortive" type. This is emphasized further by the observation that many mitotic figures at this time show signs of abnormalities. Evidence for transient increased marrow activity can be derived also from in vitro studies using H^3 thymidine as a marker for DNA synthesis. As shown in Figure 5a and b, myelocytes and erythroblasts around day 10 seem to incorporate more tritiated thymidine (method described previously (25) than do specimens obtained 4-5 months after the accident, at which time the hemopoiesis had returned to a "normal" state. Whereas the grain count over the various precursors appears to exceed the "normal" comparison values by a factor of about 2-3 in the erythropoiesis and somewhat less in the myelopoiesis, it is not certain whether there is a true increase in the percentage of labeled cells. An increased grain count under otherwise constant conditions may indicate a faster rate of DNA synthesis. If the per cent labeling remains essentially unchanged these findings could mean a shortened overall generation time. If the cells in the DNA synthesis were polyploid, the increased grain count could be explained on this basis also. However, polyploidy is not recognizable in these labeled cells.

As stated above, histological evidence for foci of myelopoietic regeneration, different in their character from the pattern of the final overall marrow

regeneration which occurs later, was found in rats exposed to 550 and 1000 r total body irradiation (13, 21). These occur about 2-3 days before the "abortive" granulocyte rise as seen in the peripheral blood. The final effective blood cell recovery of the Oak Ridge casualties was preceded in the marrow by a significant rise in the mitotic index around the 21st day after exposure (23). By the 28th day, when the blood cell counts reached minimal levels, the mitotic index in the marrow had returned to normal limits. Since it was not possible to distinguish the cytologic class of the mitotic figures, it is impossible to evaluate fully the significance of the mitotic index curve. It appears from the mitotic index curve that the onset of marrow recovery preceded the appearance of the final effective blood count rise by less than 10 days, which is compatible with time parameters estimated for human hemopoiesis (26). The maturation time from the formation of a metamyelocyte to its release as a "mature" granulocyte into the peripheral blood was estimated to require approximately 3-4 days. In the experimental rat, this final effective regeneration of the blood counts is paralleled in the marrow by reestablishment of the circulation. At the onset of cellular marrow regeneration, an increase in small round cells, conventionally called "reticulum cells" is seen which is followed by the appearance of multiple foci of regeneration around sinuses and capillaries. Occasionally sinusoidal walls were found which consisted of more than the usual one layer of flat endothelial cells to which a zone of regeneration is attached (13). This "multifocal" regeneration pattern may also be seen in the dog (18). However, regenerative areas may alternate with areas which are still completely aplastic and hemorrhagic.

3. Assessment of the severity of radiation injury from the blood and bone marrow changes; therapeutic implications:

Survival following irradiation is dependent upon successful regeneration of the bone marrow. Thus the means of predicting the probability of spontaneous regeneration would be useful to the clinician responsible for the management of irradiated human beings. From the preceding discussion the following are offered as useful criteria for the prediction of prognosis. An "abortive" rise in the leukocyte or reticulocyte counts, a "delayed" platelet curve and "abortive" mitotic recovery in the marrow have been observed in human beings who have recovered from radiation injury. Hence the presence of any of these suggests that there is a distinct statistical possibility of survival but does not assure survival. In contrast the fatal Vinca case, who was treated extensively, had a low reticulocyte count by the 5th day, low platelets by the 10th day and no "abortive" rise in the leukocytes. Despite antibiotics, transfusions of blood and marrow, he died on the 30th day after exposure. Dogs however with comparably severe radiation injury (27) have recovered when given antibiotics and transfusions of fresh blood and platelets. Accordingly, this pattern may not be uniformly fatal if some human beings can respond as favorably to therapy as dogs have.

The role of homologous bone marrow transfusions remains equivocal. Some have questioned the value of the marrow transfusions in the Vinca casualties (4,9) because the transfusions were given at a time when spontaneous recovery was to be expected (see Fig. 1). It is unlikely that marked blood cell recovery of all elements would be seen within 2-3 days after the marrow has been administered, since the maturation and differentiation of the precursor elements must occur before significant changes can be expected in the periphery (unless the amount of marrow given is comparable to the amount of bone marrow present in a normal individual) which certainly was not the case.

The evidence for useful homologous bone marrow grafts in irradiated dogs is still open to question (28,29). It has been suggested that the immunological difficulties (2nd disease) might be overcome by chemotherapy (30) but this seems unlikely to us. Before these problems are solved the application of homologous bone marrow in persons accidentally exposed to ionizing radiation should be attempted only in cases in which all other possibilities of treatment have been exhausted, and in which the serial blood and bone marrow findings indicate spontaneous marrow recovery to be remote.

Since there is no doubt that the transfusion of autologous marrow enables animals to survive lethal radiation doses up to about twice the LD₅₀ (31,32), the establishment of bone marrow banks for individuals who may be exposed to excessive doses of radiation might be considered. Considerably more work on methods of preservation and the effectiveness of such treatment in man must be done, however, and considerable thought must be given to the conditions under which such procedure might be considered warranted in addition to the hazard of general anesthesia for collection of the marrow.

At the present time, at all dose levels at which spontaneous bone marrow recovery is possible, symptomatic therapy with antibiotics, fresh blood or platelet transfusions, electrolytes etc., is still the most promising and least hazardous (9).

4. Hematologic studies indicated after possible exposure to radiation.

Ionizing radiation injury to the cells is complete upon cessation of exposure but it may take days for the marrow injury to be manifested as a clinically important depression in the peripheral blood. Irrespective of the radiation dose estimates, systematic hematologic studies are needed to assess the degree of injury and to provide guidance for therapy. These

should include at least daily blood counts (leukocytes, differential count, platelets, reticulocytes, hemoglobin, hematocrit) for an accurate determination of the slopes of the curves over the first few days. In addition, serial bone marrow aspirations with particle smears and sections will aid in the assessment of the clinical situation. The interpretation of the bone marrow findings will depend largely on the time of the aspiration after exposure. During the first 5-10 hours, special attention should be focused on the frequency of cells with karyorrhexis and karyolysis, particularly in the erythropoietic cells. The frequency appears to be a function of the dose. From 10 to 40 hours, additional and particular attention should be given to the type and frequency of "mitotically connected abnormalities." The relationship to dose is not simple: this type of abnormality is low at very high dose levels with little "abortive" regeneration and low (but without evidence of significant "direct" cell injury and without rapid cellular depletion) in the low dose ranges. It is most frequent at dose levels with a subsequent marked "transient" recovery. Difficulties arise in persons with exposure equivalent in effect to partial body irradiation. It is known that unirradiated parts of the bone marrow may enhance bone marrow recovery in an otherwise lethally irradiated organism (33-35). Under those circumstances careful observation of the trend of the blood cells appears to be most significant, in order to determine if the pattern is compatible with prospective "spontaneous marrow recovery." Also, bone marrow aspirations from different sites are helpful and may show differences as reported for the Lockport casualties (5).

Summary

The hematological data of patients of 4 radiation accidents (Rongelap 1954, Oak Ridge 1958, Vinca 1958, Lockport 1960) are reviewed and compared. The

blood cell curves appear to show three phases. 1) Initial phase (about 8-10 days). 2) Phase of "transient" or "abortive" regenerations. 3) Phase of final "effective" recovery. These phases in the blood are preceded and caused by particular events in the bone marrow. Evidence was brought forward that "transient" rises in leukocytes and reticulocytes associated with a "delayed" platelet disappearance curve are associated with a marrow capable of spontaneous recovery. In patients with inhomogenous total body irradiation, the "transient" rise may lead directly to effective recovery. Immediate decline of all blood cell elements without evidence of further, even "abortive" attempts of marrow regeneration must be considered as evidence for a "lethal" bone marrow dose and extremely serious complications may be expected. The clinical implications of these analyses are outlined and the diagnostic possibilities described.

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Figure 1: Blood cell changes (means) of 3 individuals exposed to 236-365 rads in Oak Ridge (The authors are indebted to Dr. G. Andrews for permission to use the curve for the present discussion).

FIG. 1

Figure 2: Blood cell changes of 4 individuals accidentally exposed to an inhomogeneous total body x-irradiation. (The authors are indebted to Dr. M. Ingram for permission to use the data for the present discussion.)

LOCKPORT INCIDENT, MARCH 1960

FIG. 2

Figure 3: Comparison of blood cell changes from the Rongelap accident 1954, from the Oak Ridge accident 1958, and the accident Vinca 1958 (data taken from reference No. 6). (The arrows in the lower curves indicate the time of homologous bone marrow transfusions. The initials refer to the various individuals.) The horizontal lines indicate approximate "normal limits" as assumed for Americans and Europeans, however, the "normal" values for the Marshallese are different (see text).

- a) Comparison of the platelet counts
- b) Comparison of the leukocyte counts
- c) Comparison of the lymphocytic counts
- d) Comparison of the reticulocytic counts

SERIAL PLATELET COUNTS

PLATELETS $\times 10^{-3}$ PER MM^3 BLOOD

RONGELAP ACCIDENT 4 MARCH, 1954

OAK RIDGE ACCIDENT 16 JUNE, 1958

YUGOSLAV ACCIDENT 15 OCT. 1958

SERIAL LEUKOCYTE COUNTS

LEUKOCYTES $\times 10^{-3}$ PER MM^3 BLOOD

RONGELAP ACCIDENT
4 MARCH, 1954

OAK RIDGE ACCIDENT
16 JUNE, 1958

YUGOSLAV ACCIDENT
15 OCT. 1958

SERIAL LYMPHOCYTE COUNTS

FIG. 3(d)

Figure 4: Schematic outline of the effects of a single dose of total body radiation on myelopoiesis or erythropoiesis. After a single dose, cells may proceed with normal proliferation and maturation (lower half of diagram). Result: 8 normal end cells. Or: Nuclear division may be inhibited and all may go through maturation without further division. Result: depending on the level of damage instead of 2,4,8 or 16 cells only one "end cell". Or a cell may be damaged with immediate cell death: depending on stage this may result in 4, 8, or 16 fewer "end cells." The immediate result of irradiation on a hemopoietic cell population is either a complete block of all further production, or "ineffective" hemopoiesis as a function of dose.

Mitotically connected cell injury and its effect on the effective blood cell production

Figure 5: In vitro incubation with tritiated thymidine, of bone marrow cells from the Oak Ridge casualties, Days = after radiation accident.

- a) Erythropoiesis: E2 "early basophilic" erythroblast, E3 basophilic normoblast, E4 polychromatic normoblast, E5 oxyphilic normoblast.
- b) Myelopoiesis: M2: promyelocyte, M3 large myelocyte, M4 small myelocyte.

IN VITRO LABELING OF ERYTHROPOIESIS WITH
H³T AFTER RADIATION INJURY

FIG. 5(a)

IN VITRO LABELING WITH H^3T OF MYELOPOIESIS
AFTER RADIATION INJURY