Patterns of neuroglial proliferation in spinal cord white matter following exposure to ionizing radiation

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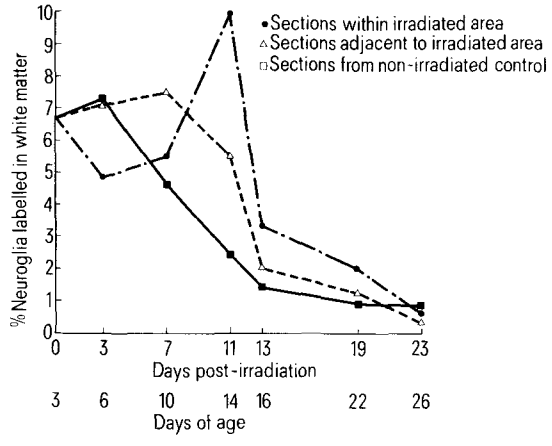
Summary. X-irradiation temporarily decreases the proliferative activity of neuroglia in immature rat spinal cord. Later, the proliferative activity in these irradiated regions surpasses that noted in control rats. Areas adjacent to the irradiated region have a greater than normal percentage of labelled neuroglia and may also be a source for neuroglia which re-populate the irradiated zone.

X-irradiation (2000–4000 R) of lumbosacral spinal cords in 3-day-old rats alters the normal development of neuroglia and, consequently, of myelin[2–5]. Exposure to 4000 R not only affects neuroglia and myelin but can also result in focal necrosis with loss of neural tissue[2–5]. When the exposure is limited to 2000 R, however, there is usually only a transient state of neuroglial hypoplasia and a delay in myelinogenesis with no other tissue alteration[4]. This state of decreased neuroglial number and hypomyelination was noted at 11 days post-irradiation, whereas by 3–4 weeks post-irradiation the spinal cords appeared to be normal. Since only a 5 mm length of lumbosacral spinal cord had been exposed to ionizing radiation and since a few neuroglia remained in the irradiated area, there were at least 2 possible sources for the neuroglia that eventually repopulated the irradiated area. First, these cells could have developed by proliferation of the neuroglia that remained in the irradiated area. Second, neuroglia in the adjacent nonirradiated area could have proliferated and migrated into the irradiated region. The present study was undertaken 1. to evaluate the proliferative capacities of the neuroglial population in the irradiated and adjacent nonirradiated areas and 2. to compare them with proliferative capacities of the neuroglial population from comparable areas of spinal cords in nonirradiated, control rats.

Materials and methods. 3-day-old Charles River CD® rats were irradiated and were killed at intervals up to 23 days post-irradiation. 3 irradiated and 2 nonirradiated rats were perfused at each interval. The rats received a single dose of 2000 R of soft X-rays from a Philips contact therapy apparatus. The irradiation conditions and the methods for restraining the animals and limiting the exposed area to lumbosacral spinal cord have been described in detail elsewhere[6–8]. 2 h prior to perfusion-fixation each animal was injected i.p. with ^{3}H-thymidine (2μCi/g b.wt, Amersham; sp. act. 5 Ci/mM). Autoradiographs of spinal cord sections were prepared by the dipping technique using Kodak NTB 2 emulsion. Both labelled and non-labelled neuroglia were enumerated in the white matter of the irradiated and the adjacent nonirradiated areas in the irradiated rats and in comparable segments of spinal cord in nonirradiated control rats. At least 2 but usually 3 sections were counted from each area of interest. The counts were made independently by 2 individuals, and the percentage of labelled neuroglia was calculated.

Results and discussion. The percentage of labelled neuroglia in relation to age and to days post-irradiation is shown in the figure. In the case of the normal, nonirradiated animals, there was a consistent decrease in the percentage of neuroglia that was labelled after the 1st week of age. This pattern is essentially the same as that reported previously by this investigator[9]. In contrast, exposure to X-rays markedly reduced the percentage of labelled neuroglia observed in the irradiated area at 3 days post-irradiation. By 7 days post-irradiation this population began to rise and increased to nearly 10% during the 2nd post-irradiation week. By the end of that week, however, the proportion of neuroglia labelled decreased markedly. Thereafter, this decrease continued gradually and approached normal levels during the 3rd post-irradiation week. The neuroglial population in sections immediately adjacent to the irradiated area showed little change in the proportion of cells labelled during the 1st post-irradiation week; hence, by the end of that week the percentage of labelled neuroglia in sections adjacent to the irradiated area was greater than would be anticipated for that age (10 days) in nonirradiated controls and in the irradiated area. This increased percentage of labelled neuroglia in sections adjacent to the irradiated area over that occurring in nonirradiated controls persisted until the end of the 2nd post-irradiation week. Thereafter, the percentage of cells labelled in sections adjacent to the irradiated area did not differ markedly from that observed in nonirradiated control rats.

These data indicate that although radiation initially inhibits the normal proliferative activities of neuroglia in the white matter, this inhibition is followed by a marked increase in the population of labelled cells. In addition, the adjacent, nonirradiated areas have a higher than normal proportion of labelled cells in the neuroglial population, suggesting that there may be a stimulus from the hypocellular, hypomyelinated areas which induces proliferation of neuroglia which could then migrate into the irradiated area. It is not possible, however, in the present study to determine the sites of origin of cells that re-populate the irradiated area.



Percentage of neuroglial cells labelled in white matter of spinal cords in rats in relation to age and to radiation status.

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