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Life Shortening by Multiple Doses of Irradiation

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There is currently a widespread belief that radiation can accelerate the normal process of ageing in mammals, although there is no evidence that life shortening in man following multiple doses of irradiation has been due to anything but the induction of specific diseases. The original report that the duration of life of American radiologists was less than would have been expected has been shown to be due to a fallacy in interpretation (Seltser and Sartwell, 1958). On the other hand radiotherapy can shorten life by causing radiation "pneumonitis", radiation "nephritis", and a variety of cancers, and occupational exposure to radiation has caused such specific diseases as cancer of the lung, bone and skin as well as leukaemia.

Single large doses of radiation are known to kill in a few days or weeks. Animals surviving this period of acute deaths die sooner than do unirradiated controls, and the wide variety of pathological phenomena which such irradiated animals show may be quantitatively interpreted as the result of premature ageing (Upton, 1957, 1959). However, it is a logical mistake to think that an investigation of the mechanism of damage by single large doses necessarily helps to explain the effect of multiple doses of any toxic agent (Mole, 1959a).

Many experimental variables need consideration when the delayed effects of multiple doses of irradiation are examined, such as the duration of the period of irradiation and the dose-intensity

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of individual exposures as well as the normal life span of the kind of animal used and its normal incidence of killing diseases. There may well be a 10 per cent difference in mean survival time of groups of unirradiated controls in different experiments over the course of several years, so that small differences should not be regarded as established until the experiments have been repeated, a lengthy business. With mice there are often markedly curvilinear dose-response curves and sometimes quite unexpected results, such as the finding that giving a fixed total dose of radiation over a longer period of time may increase the life shortening effect, or that increasing the duration of an exposure to daily irradiation (and therefore the total dose) beyond a certain point may produce very little increase in effect (Mole, 1959b). Increasing the age of the animals at the start of the irradiation may reduce the apparent life shortening effect. The results, in fact, seem to depend principally not so much on non-specific ageing as on whether specific consequences of radiation, such as mouse leukaemia, occur.

Summary The hypothesis that non-specific ageing is caused by exposure to multiple doses of irradiation is criticized. Clinical and experimental results show that life shortening following such exposures is commonly due to specific consequences.

Zusammenfassung

Die Hypothese, daß durch mehrfache Dosen von Bestrahlung ein unspezifisches Altern verursacht werde, wird kritisiert. Sowohl die klinischen wie die experimentellen Befunde zeigen, daß die Verkürzung der Lebenszeit, die auf solche Bestrahlungen eintritt, gewöhnlich durch spezifische Wirkungen verursacht wird.

Resume

L'auteur critique l'hypothèse selon laquelle un vieillissement non spécifique serait cause par l'irradiation répétée.

Les résultats cliniques et expérimentaux montrent plutôt que le raccourcissement de la durée de vie observée est imputable à des causes pathologiques définies.

References

Mole, R. H.: Some aspects of mammalian radiobiology. *Radiat. Res. Suppl.* 1; 124-148 (1959 a).

– Effects of dose-rate and protraction: a symposium. 1. Patterns of response to whole-body irradiation: The effect of dose intensity and exposure time on duration of life and tumour production. *Brit. J. Radiol.* 32: 497-501 (1959b).

Seltser, R. and Sartwell, P. E.: Ionizing radiation and longevity of physicians. *J. Amer. med. Ass.* 166: 585-587 (1958).

Upton, A. C: Ionizing radiation and the aging process. *J. Geront.* 12: 306-313 (1957).

Upton, A. C: Ciba Foundation Lecture, London, July 1959.