

Buckton K E, Jacobs P A, Court Brown W M & Doll R. A study of the chromosome damage persisting after X-ray therapy for ankylosing spondylitis. *Lancet* 2:676-82, 1962. [MRC Clinical Effects of Radiation Res. Unit, Western Gen. Hosp., Edinburgh, Scotland and MRC Statistical Res. Unit, Univ. Coll. Hosp. Med. Sch., London, England]

Immediately after radiotherapy for ankylosing spondylitis (total dose 1,500 r), 32 percent of lymphocytes carried unstable chromosome abnormalities, which gradually disappeared at a rate of 3.5 percent per month. The frequency of cells with stable chromosome abnormalities did not change with time posttreatment. [The SCI® indicates that this paper has been cited in over 275 publications since 1962.]

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"This study was initiated by the late Court Brown, who, with his colleague (now Sir) Richard Doll, had made a detailed study of the incidence of leukaemia and other cancers in irradiated ankylosing spondylitis (AS) patients. He felt that 'a knowledge of the effects of radiations at the cellular and subcellular levels might provide clues to the mechanism of leukaemogenesis'; one such subcellular level was the human chromosome. The technique for obtaining chromosome preparations from human peripheral blood, which became available in 1960,<sup>1</sup> was a further stimulus to investigate *in vivo* radiation-induced chromosome damage in man. The AS patients were chosen because of the wealth of knowledge of the long-term effects of irradiation and because the disease, which primarily affects men usually as young adults, is not itself malignant. As our group had its premises in a small part of the department of radiotherapy, the patients were receiving their treatment and at-

tending the follow-up clinics nearby, and therefore were readily available.

"The publication was criticised by one radiation cytogeneticist because it introduced a new classification of different types of chromosome aberrations of which he did not approve. Although we no longer use the nomenclature, the terms 'unstable' and 'stable' aberrations, which were also introduced in this paper, have now been widely accepted.

"This publication was followed by more extensive studies of the radiation-induced chromosome aberrations in AS patients, but it laid the grounding for the direction of future studies and was the first indication that this damage remained in the body for many years posttreatment. As the blood culture technique was fairly new at the time this study was done, we were not aware of a number of pitfalls surrounding the system, and particularly the timing of the first divisions in culture, which led us to suggest that 'many of the cells with unstable abnormalities have divided *in vivo*.' Later studies<sup>2</sup> showed that the majority of cells had divided *in vitro* by three days in culture and this was the reason for dicentricity being present without their accompanying fragments or with two similar fragments.

"As a result of this study, it was realised (1) that there was a population of lymphocytes with a much longer life cycle than had previously been estimated;<sup>3</sup> (2) that chromosome aberrations could be used as a 'biological dosimeter' of both partial and whole body irradiation, even if the irradiation had taken place some years previously;<sup>4</sup> and (3) that the age of the individual at irradiation might be an important factor to be taken into consideration.

"I believe that this paper has been highly cited because it was of interest not only to cytogeneticists, but also to radiation biologists, epidemiologists, and immunologists."

1. Moorhead P S, Nowell P C, Mellman W J, Battips D M & Hangerford D A. Chromosome preparations of leucocytes cultured from human peripheral blood. *Exp. Cell Res.* 20:613-16, 1960.
2. Buckton K E & Pike M C. Time in culture. An important variable in studying *in vivo* radiation induced chromosome damage in man. *Int. J. Radiat. Biol.* 8:439-52, 1964.
3. Buckton K E, Smith P G & Court Brown W M. The estimation of lymphocyte lifespan from studies on males treated with X-rays for ankylosing spondylitis. (Evans H J, Court Brown W M & McLean A S, eds.) *Human radiation cytogenetics*. Amsterdam: North Holland, 1967. p. 106-14.
4. United Nations. Scientific Committee on the Effects of Atomic Radiation. *Report of the United Nations Scientific Committee on the Effects of Atomic Radiation*. New York: UN, September 1969. 165 p. Document A/7613.