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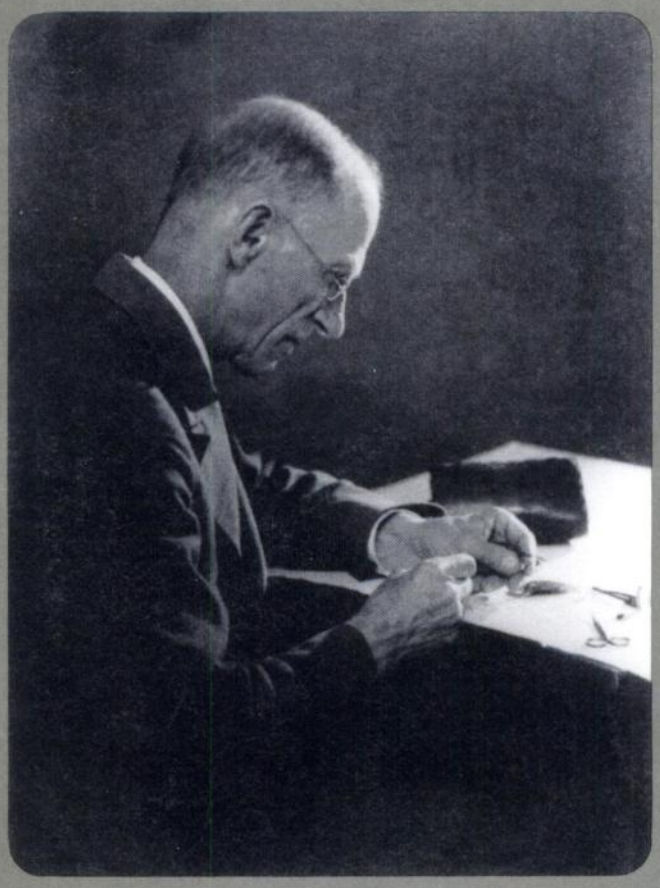

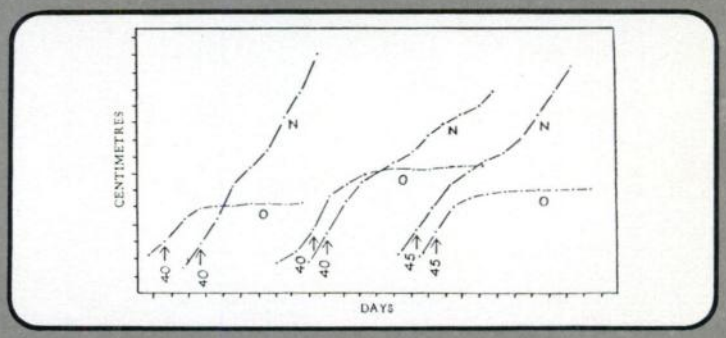

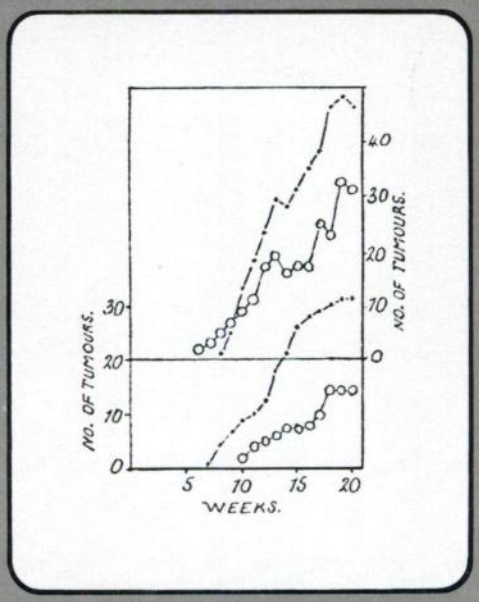

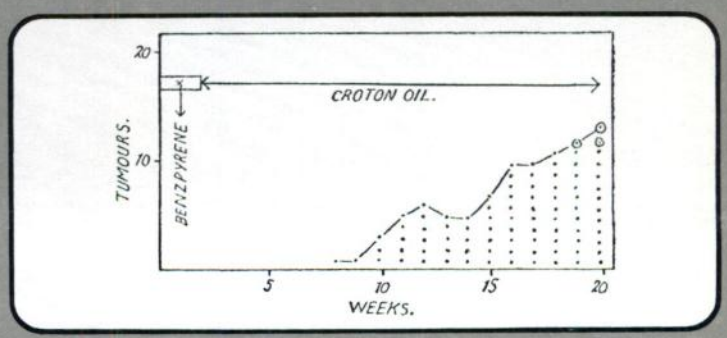

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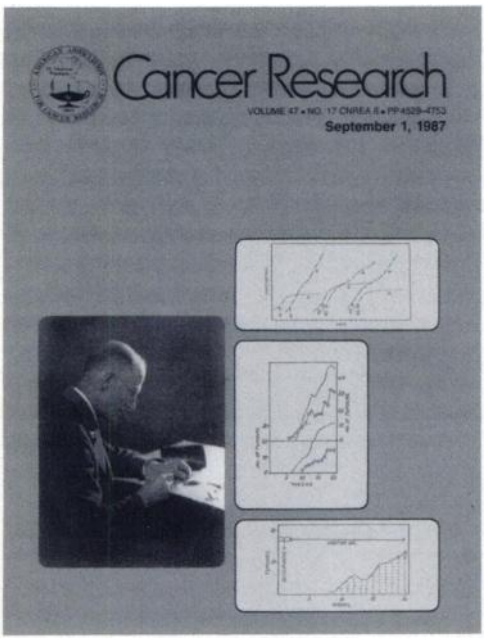

The cover honors James Cecil Mottram (1880–1945), a pioneer British experimentalist in radiobiology and chemical carcinogenesis. He pursued his research in three English institutions: the Middlesex Hospital (1908–1919); the Radium Institute, London (1919–1937); and the Mount Vernon Hospital, Northwood, Middlesex (1937–1945).

Mottram confirmed and extended the observations of Crabtree and Cramer (Proc. Roy. Soc., 113–226, 1933) on the diminished susceptibility of cells to ionizing radiation under anaerobic conditions. Mottram found that oxygen increases the sensitivity of cells to ionizing radiation. He investigated this effect in detail at the cellular level with bean roots in which he recognized that oxygen acts essentially during irradiation (Br. J. Radiol., *8:* 32–39, 1935). He found an oxygen effect with skin and tumors and was quick to appreciate its relevance to radiotherapy because tumors were liable to have regions of hypoxia. Mottram's pioneering work on radiosensitization by oxygen was continued, and greatly extended, by L. H. Gray, who had joined Mottram's department to explore the role of neutrons in radiotherapy.

Mottram's studies in chemical carcinogenesis were preceded by his findings that exposures of *Paramecia* to benzo(*a*)pyrene increased the formation of abnormal progeny (Cancer Res., *1:* 313–323, 1941). In the year before his death he noted (J. Pathol. Bacteriol., *56:* 181–187, 1944) that even a single dose of 60 μg of benzo(*a*)pyrene was sufficient to induce tumors in the skin of mice if followed by repetitive doses of croton oil. Neither of these treatments alone induced tumors. This use of very limited doses of carcinogen confirmed and extended earlier work on stages of carcinogenesis by Berenblum (Cancer Res., *1:* 807–814, 1941) and was important in the later studies of Berenblum and Shubik (Br. J. Cancer, *1:* 379–382 and 383–391, 1947) on two-stage carcinogenesis (initiation and promotion) in mouse skin.

Mottram also found a diurnal variation in the production of tumors in mouse skin by a single application of benzo(*a*)pyrene (J. Pathol. Bacteriol., *57:* 265–267, 1945). Tumor formation was approximately twice as great when mouse skin was exposed to the carcinogen at midnight than at midday. The opposite diurnal variation was known to occur in the frequency of mitoses in mouse skin. Later Frei and Ritchie (J. Natl. Cancer Inst., *32:* 1213–1220, 1964) confirmed the diurnal variation in tumor formation reported by Mottram and further showed that the number of epidermal cells duplicating DNA is approximately 4-fold greater around midnight than around noon. Thus the carcinogen appears to act on cells synthesizing DNA.

In the last few years of his life Mottram also collaborated with F. Weigert on the complex metabolism of benzo(*a*)pyrene in skin and its relationship to carcinogenesis by this hydrocarbon. An obituary of Mottram may be found in the *British Journal of Radiology, 19:* 347–348, 1946.

Three of Mottram's experiments are pictured. *Top:* Effect of oxygen (O) and of nitrogen (N) upon the growth of three pairs of beans exposed to X-rays (1935). *Center:* Tumors on right flank of mice, which was painted with benzo(*a*)pyrene every second day for 14 days, followed by croton oil three times weekly. The left flank, painted with benzo(*a*)pyrene only, has no tumors (1944). *Bottom:* Tumor yield in mice painted with benzo(*a*)pyrene at midday (*circles*) and at midnight (*dots*), showing diurnal effect (1945).

We are indebted to Drs. James A. Miller and Peter Alexander for the information and to Mottram's son, Jim Mottram, Milford-on-Sea, Hampshire, England, for the portrait, in which Mottram's expertise as a fly fisherman is emphasized.

M. B. S.