Eur J Cancer Clin Oncol, Vol. 19, No. 6, pp. 859–860, 1983.
Printed in Great Britain.

0277-5379/83$3.00+0.00

Letter to the Editor

Adolescent Bone Cancer: is the Growth Spurt Implicated?

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BONE cancer exhibits an unusual age-incidence pattern, with peak incidence occurring in adolescence [1–6]. Many investigators have suggested a correlation between growth rate and the incidence rate of adolescent bone cancer [2–7]. Close inspection, however, does not support such a correlation: (1) rate of growth is maximal during the fourth month of gestation and even between birth and age 2 yr, the rate of growth exceeds that at the peak of the adolescent growth spurt [8, 9], but the incidence of bone cancer is minimal below 2 yr of age [1–6]; (2) the incidence of bone cancer begins to increase in childhood [1–6] well before the beginning of the adolescent growth spurt and at a time when growth is slow [8, 9]; (3) the incidence of bone cancer remains substantial after age 20 yr [2], when growth becomes negligible [8, 9].

It is possible to imagine that neoplastic mutations accumulate during rapid proliferation of bone cells in gestation and infancy and are then promoted by the adolescent growth spurt [10, 11]. But such theories are subtle, complicated and unsubstantiated at present. In addition, any theory advocating a causal relationship between the rates of growth and bone tumor incidence must ultimately account for the lack of correlation between rates of growth and tumor incidence in tissues other than bone. Many tissues participate in gestational and adolescent growth spurts [8, 9], but only bone exhibits peak tumor incidence in adolescence. We conclude that rate of growth is inadequate as an explanation for, and may be irrelevant to, the unique age-incidence pattern for bone cancer. This conclusion is supported by the identical growth rates exhibited by patients with osteosarcoma and their healthy identical twins [12]. In addition, Ewing's sarcoma is almost absent in blacks [13]. The strong racial difference in frequency of occurrence of Ewing's sarcoma argues against an etiologic mechanism, such as growth rate or bone reconstruction, which is racially indistinct.

Cells are most susceptible to mutation during genome replication [14]. If the age-incidence pattern for bone cancer was determined primarily by the susceptibility of bone cells to neoplastic mutation, the age-incidence pattern for bone cancer might correlate with the rate of bone cell proliferation, i.e. with growth. The fact that such a correlation is not obvious suggests that the susceptibility of bone cells to mutation is not the dominant determinant of the unique age-incidence pattern. This suggestion is supported by the finding that no age from infancy through adolescence was more or less vulnerable to radiation-induced bone carcinogenesis [15].

Adolescent bone cancer is more common in males than in females [1–3, 5, 6, 16]. This is consistent with positive correlations between stature and bone tumor incidence which have been observed in humans [4, 7] and in dogs [17]. But the correlations are unlikely to be a consequence of differences in growth rates. Stature itself is a measure of the number of targets for carcinogenic events and thus represents a sufficient explanation for the correlations with bone tumor incidence [16].

We have concluded previously that susceptibility to neoplastic mutation is the dominant determinant of the age-incidence patterns for the vast majority of human cancers [18–20]. This explanation is unlikely to apply to bone cancer.

Accepted 19 November 1982.

We suggest that the neoplastic mutagenicity of the bone environment, e.g. viruses [21], is likely to be the dominant determinant of the adolescent incidence peak for bone cancer.

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