THE INCIDENCE OF MALIGNANT PRIMARY BONE TUMOURS
IN RELATION TO AGE, SEX AND SITE
A Study of Osteogenic Sarcoma, Chondrosarcoma and Ewing’s Sarcoma
Diagnosed in Sweden from 1958 to 1968

SVEN-ERIK LARSSON and RONNY LORENTZON, UMEA, SWEDEN
From the Department of Orthopaedic Surgery, University of Umeå

In a previous investigation (Larsson and Lorentzon 1974) on the geographical variation
of the incidence of malignant primary bone tumours, osteogenic sarcoma, chondrosarcoma
and Ewing’s sarcoma were found to show a striking similarity in the pattern of variation
of the factors studied. Thus, all three tumours showed a significantly higher incidence in the
southern part of Sweden than in the rest of the country. Males showed a significantly higher
incidence than females. Interestingly, both osteogenic sarcoma and chondrosarcoma showed
the highest incidence among males of the urban population in almost all parts of the country.
In contrast, Ewing’s sarcoma showed the same incidence among the urban and rural population.
The present study was undertaken in order to obtain further information on factors related
to the incidence of these tumours.

In studies of bone tumour mortality for England and Wales the incidence of osteogenic
sarcoma has been related to changes in growth velocity at the adolescent growth spurt and,
at high age, to Paget’s osteitis deformans (Price 1955, Hems 1970). For the Japanese population
(the National Cancer Centre in Tokyo 1966) the same adolescent peak has been reported as
for the British population but no increase after forty years of age. These circumstances might
be related to the absence in Japan of Paget’s disease, which has been reported to be of importance
as a precancerous condition in relation to bone tumours in Britain (Sissons 1966). There is
clearly a need for more information of this sort from populations living in different parts of
the world.

METHODS

A comparative analysis of osteogenic sarcoma, chondrosarcoma and Ewing’s sarcoma
was made with regard to specific age incidence in relation to the sites of the tumour, to sex
and to growth velocity. From the Cancer Registry, National Board of Health and Welfare
in Sweden, it was possible to obtain complete information for all registered new cases of
primary bone tumours diagnosed in Sweden from 1958 to 1968.

| TABLE 1 |
| --- | --- |
| **CLASSIFICATION OF MATERIAL** |  |
|  | Number | Per cent |
| Osteogenic sarcoma | 242 | 28.8 |
| Chondrosarcoma | 193 | 22.9 |
| Ewing’s sarcoma | 74 | 8.8 |

Since 1958 all cases of malignant neoplasm throughout the country have been reported to
the Cancer Registry at the time of diagnosis. When a case is reported to the Registry, the
certifying doctor always gives certain details such as the age and sex of the patient, whether
the patient is a twin or not, place of living, occupation, hospital, whether the diagnosis is
based upon histopathological examination of biopsy material or not, and, if this is the case,
the exact histopathological diagnosis, the affected skeletal part, the eventual presence of metastases and, finally, whether treatment has been instituted or not. In the present study the data were obtained by computer-aided search in the Registry.

The histopathological typing of the tumours and nomenclature followed the system established by The World Health Organisation International Reference Centre for the Histological Definition and Classification of Bone Tumours (1972). As found in a previous study on Ewing's sarcoma (Larsson, Boquist and Bergdahl 1973), the diagnosis was apparently made with a high degree of accuracy.

**MATERIAL FOR STUDY**

During the eleven-year period 1958–68 a total of 832 cases of malignant primary bone tumour were diagnosed. Out of these, 16·2 per cent were unspecified, 10·6 per cent having a diagnosis based upon radiological or clinical examination only and 5·6 per cent having a diagnosis of "sarcoma" without any further classification of the tumour. In the remaining 83·8 per cent of the cases the diagnosis was based upon histopathological examination of biopsy material. The study material constituted the following number of specified cases with respective figures given also in per cent of the total number of malignant bone tumours diagnosed (Table 1).

**RESULTS**

**Tumour site and sex distribution**—Figure 1 shows the distribution of the studied tumours according to site and sex. All three tumours showed a predominance for males, giving the following ratios for males to females: for osteogenic sarcoma 1:40 to 1; for chondrosarcoma 1:38 to 1; and for Ewing's sarcoma 1:96 to 1. However, when the various tumour sites were considered, only Ewing's sarcoma was consistently found to show the same predominance of males over females. For osteogenic sarcoma and chondrosarcoma this relationship between the two sexes was found only for localisation of the tumour to the long bones of the lower limb, the pelvis, vertebrae and, to some extent, the long bones of the upper limb and scapula. In fact, the striking preponderance of males to females was mostly due to tumours localised to the long bones of the lower limb, the pelvis and vertebrae, found both for osteogenic and chondrosarcoma with sex ratios for these localisations of 1:60 to 1 and 1:86 to 1 respectively. The incidence for the other tumour sites did not show such a difference between the two sexes, with ratios of 1:00 to 1 and 1:02 to 1 respectively for osteogenic sarcoma and chondrosarcoma. Although the predilection sites for osteogenic sarcoma and chondrosarcoma were different, the sex ratios showed a strikingly similar variation pattern for the two types of bone tumour.

![Diagram of tumour site distribution](image)

**Fig. 1**

The total numbers of osteogenic sarcoma, chondrosarcoma and Ewing's sarcoma diagnosed in Sweden 1958–68 and their distribution according to sex and site.
Age specific incidence—The incidence for osteogenic sarcoma and Ewing's sarcoma showed a typical peak during adolescence (Fig. 2). Osteogenic sarcoma showed an incidence for the ages of fifteen to twenty years approximately three times higher than for the ages above sixty-five years. Whereas Ewing's sarcoma was very rare after the age of twenty-five years, the incidence of osteogenic sarcoma showed a successive increase with increasing age that almost paralleled that of chondrosarcoma. The adolescent peak for osteogenic sarcoma was found to be caused by the very high incidence of tumours being localised to the long bones of the lower limb at this age (Fig. 2). Chondrosarcoma showed a peak incidence for the ages of seventy to seventy-five years that was almost as high as the adolescent peak for osteogenic sarcoma.

Incidence of osteogenic sarcoma in relation to growth velocity—The adolescent peak for tumours of the long bones of the lower limb occurred at the age of twelve years and five months for females and sixteen years and seven months for males, showing a close coincidence with the accelerated growth velocity for the two sexes at corresponding ages (Fig. 3). When the material was subdivided, a large peak appeared for the juvenile group from birth to thirty-four years, a small peak for the intermediate group aged thirty-five to forty-nine years and a somewhat larger peak for the senile group aged fifty years and over. For the other sites (Fig. 4), a relatively low incidence of the tumour was found. None of the sites showed a typical adolescent peak.

Chondrosarcoma—The various tumour sites showed almost similar incidence patterns (Fig. 5). The incidence was very low during childhood and showed a successive increase with age for all sites and for the two sexes.

Ewing's sarcoma—In contrast to osteogenic sarcoma, the typical adolescent peak for Ewing's sarcoma occurred at the same age for males and females (Fig. 6). Thus, the incidence of Ewing's sarcoma could not be related to the adolescent growth spurt.

DISCUSSION

The total malignant bone tumours diagnosed in Sweden from 1958 to 1968 constituted 0.4 per cent of all malignant neoplasms (Larsson and Lorentzon 1974). The 242 osteogenic sarcomas comprised 28.8 per cent of the malignant bone tumours which should be compared to the corresponding figure of 21.9 per cent reported by Dahlin (1967) for the Mayo Clinic material. The difference might be due to the fact that the material of the present study represents the natural occurrence of these tumours within a homogenous population of a whole country, contrary to that of the Mayo Clinic. Furthermore, there might be geographical or racial variations. Thus, considerably higher figures have been reported in series from Canada (Phillips 1965) and from England and Wales (Boyd, Doll, Hill and Sissons 1969) with 50 and 40 per cent respectively. In these papers the estimates of incidence came indirectly from
mortality data which might explain the high figures. The relative frequency of chondrosarcoma was 22.9 per cent in the present material and only 11 per cent in the series reported from the Mayo Clinic (Dahlin 1967) and from England and Wales (Boyd and colleagues 1969). In comparison with these papers, Ewing's sarcoma showed a slightly higher relative frequency in the present series. Overall, it appears from these various reports that more exact information on the natural occurrence of these malignant tumours is needed to allow any direct comparisons to be made with regard to variations in incidence between different populations.

In the present investigation, the adolescent incidence peak for osteogenic sarcoma was found to be caused by tumours localised to the long bones of the lower limb. For these tumours, the peak incidence was at a mean age of twelve years and five months for girls and sixteen years and seven months for boys. It showed a very close coincidence with the maximum growth velocity for the adolescent growth spurt which has been reported to occur at the age of twelve years for females and fourteen years for males (Tanner, Whitehouse and Takaishi 1966). The incidence of osteogenic sarcoma for these bones could also be correlated with the sex difference in the mean bone volumes reported by Vallois (1957). A similar relationship between age, sex and site distribution of osteogenic sarcoma and bone growth and maturation during adolescence has been reported for a series from England (Price 1955). Bone cancer mortality in the young in England and Wales was similarly found to be correlated with changes in growth velocity at the adolescent growth spurt for males and females (Hems 1970). Osteogenic sarcomas showing localisations other than the long bones of the lower limb were randomly distributed among all ages in the present material.

In the present series Ewing's sarcoma showed no sex difference with regard to its incidence peak in contrast to osteogenic sarcoma, although the adolescent incidence peaks for both tumours showed a striking coincidence. The nature and origin of Ewing's sarcoma is still debated. Ewing (1921) described it as an "endothelial myeloma" and it is now classified as a marrow tumour (Schajowicz, Ackerman and Sissons 1972). Its clinical course, radiosensitivity and the lack of a favourable effect of radical surgical treatment (Larsson and colleagues 1973) also seem to justify the classification of this tumour as a marrow tumour rather than as a tumour primarily of bone.

In the present series the incidence of osteogenic sarcoma in patients over the age of thirty years ran parallel with that of chondrosarcoma, thus showing a successive increase with increasing age. The specific age incidence was three times higher among individuals aged fifteen to twenty years than in those aged sixty to eighty-five years. The same relationship was found in the American series by Geschickter and Copeland (1949), while in the British series this feature was reversed by a factor of four in the juvenile to five in the senile group (Price 1955).
The age specific incidence of osteogenic sarcoma in males and females for tumours with localisations other than to the long bones of the lower limb.

The age specific incidence of chondrosarcoma according to sex and site.
This difference appears to be related to the association of osteogenic sarcoma with Paget's disease, which is relatively common in Britain but uncommon in the United States of America and in Scandinavian countries (Sissons 1966). In the present investigation, osteogenic sarcomas of the long bones of the lower limb were found to be 1.6 times as common as in all other localisations and 4.6 times more frequent than in the long bones of the upper limb and scapula. This corresponds well with the figure of 4.2 reported by Dahlin (1967). Since in the dog osteogenic sarcoma is 1.6 times more frequent in the fore limb than in the hind limb, weight-bearing has been claimed to be of importance as an etiological factor (Wolke and Nielsen 1966). In the present study, the long bones of the lower limb, the pelvis and the spinal column showed a particular feature in that

the sex ratio for both osteogenic sarcoma and chondrosarcoma showed the characteristic predominance of males over females for these sites only but not for other localisations. This relationship was not found for Ewing's sarcoma. Weight-bearing might possibly modify the cellular response of the bone tissue to some external causative agent, like viruses. A common virus etiology for bone sarcomas has been suggested (Moore 1971). Common antibodies against intracellular antigen from osteogenic sarcoma, chondrosarcoma, fibrosarcoma and giant-cell tumour have been demonstrated (Moore and Price 1970). Epidemiological studies of individuals having this specific antibody have shown that disease is not an invariable consequence of infection (Morton and Malmgren 1968). In the etiology of bone sarcomas, internal factors such as age, sex, and bone growth and maturation thus appear to be of importance in modifying the response of the tissue to causative external factors like viruses.

**SUMMARY**

1. The incidence of osteogenic sarcoma, chondrosarcoma and Ewing's sarcoma in relation to age, sex and site is analysed in a study of 832 malignant primary bone tumours diagnosed in Sweden in 1958–68. The results are compared with those in other series.

2. The adolescent incidence peak for osteogenic sarcoma is caused by tumours localised to the long bones of the lower limb. The peak incidence occurs at a mean age of twelve years for girls and sixteen years for boys and is associated with the maximum growth velocity for the adolescent growth spurt.
3. Ewing's sarcoma, showing no sex difference with regard to its incidence peak, seems not to be associated with bone growth.

4. In the adult, the incidence of osteogenic sarcoma parallels that of chondrosarcoma, thus showing a successive increase with increasing age. In Sweden, where Paget's disease is uncommon, the incidence of osteogenic sarcoma over the age of thirty is only one-third of that during adolescence.

5. In osteogenic sarcoma and chondrosarcoma but not in Ewing's sarcoma, the characteristic predominance of males over females is valid only for localisations to the long bones of the lower limb, the pelvis and the spinal column and not for other sites. Internal factors such as age, sex, bone growth and maturation and also weight-bearing seems to be of importance in modifying the response of the tissue to a causative external factor, like a common virus.

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REFERENCES


