Embryonal sarcoma and embryonal rhabdomyosarcoma of the orbit

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SYNOPSIS A series of 34 cases of embryonal sarcoma and embryonal rhabdomyosarcoma of the orbit has been placed histologically into three groups according to their maximum degree of differentiation at any stage: (a) embryonal sarcoma, (b) non-striated embryonal rhabdomyosarcoma, and (c) striated embryonal rhabdomyosarcoma. The patients were then followed up. This paper presents a summary of the clinical course of the whole series and an account of eight typical cases; the age and sex incidence and survival rates are shown and the histology, treatment, and prognosis are discussed.

Attention was first directed towards the importance of rhabdomyosarcoma of the orbit by Reese and Calhoun in 1941, and since that time the condition has been recognized with increasing frequency (Forrest, 1949; Stobbe and Dargeon, 1950; Eibergen, 1952; Stout, 1953; Paufique and Etienne, 1955; Lederman, 1956; Blodi, 1956; Slem, 1957; Blaxter and Smith, 1958; Horn and Enterline, 1958; Vanneste and Bernolet, 1958; Farra, 1959; Frayer and Enterline, 1959; Moore and Grossi, 1959; Hervouet, Francois, Dabov and Lenoir, 1960; Santino, 1960; Shafto, 1960; Offret and Haye, 1961; Illif and Ossofsky, 1962; Spaeth and Cleveland, 1962; Porterfield and Zimmerman, 1962). Over 100 cases have now been reported, the largest series consisting of 55 cases (Porterfield and Zimmerman, 1962), and it has become apparent that rhabdomyosarcoma is not only the commonest primary malignant tumour of the orbit in childhood, but that the orbit is also the commonest site of this neoplasm (Frayer and Enterline, 1959; Porterfield and Zimmerman, 1962).

As originally pointed out by Bard (1885) and subsequently by many other workers, rhabdomyosarcomata may be roughly grouped into two main categories, (a) adult forms and (b) embryonal forms. In the first group the neoplasm arises from voluntary muscle and is therefore correctly classified histogenetically as a rhabdomyosarcoma. Typically it occurs in adult life, with a mean age incidence of about 40 years (Stout, 1946) and is extremely rare, the fully mature muscle cell not being prone to neoplastic change. In their series of 55 cases of orbital rhabdomyosarcomata, Porterfield and Zimmerman (1962) identified no tumour of this type, although Reese (1963) felt that some of their more 'differentiated' cases might be so classified.

The second group is more common and occurs in children and adolescents, the growth tending to arise in particular sites and most commonly where no striated muscle is normally present, as in the genito-urinary or biliary passages (Horn, Yakovac, Kaye, and Koop, 1955). These tumours apparently originate in embryonic mesenchymal tissue which is either prospective muscle or undifferentiated mesenchyme capable of heteroplastic muscle differentiation (Willis, 1948; 1958), and cannot, therefore, be strictly classified on a histogenetic basis as rhabdomyosarcoma. It is usual to call them embryonal sarcoma or embryonal rhabdomyosarcoma, although histologically they may be indistinguishable from the adult type of rhabdomyosarcoma, as shown in the study of Phelan and Juardo (1962).

Some pathologists prefer to reserve the term embryonal rhabdomyosarcoma for those neoplasms where definite cross-striations may be demonstrated (Lorenz, 1904; Constance, 1955; Ashton, 1958), while others believe that the rhabdomyoblast is sufficiently characteristic to be recognized without cross-striations, describing all these tumours as rhabdomyosarcomata whether cross-striations are found or not (Genevet, 1900; Rakov, 1937; Ober, Palmer, and Glassy, 1953).

It is true that these tumours behave in a very similar fashion irrespective of cross-striations, the demonstration of which in many cases depends upon the diligence with which they are sought; moreover,
although absent in the primary growth, cross-stria-
tions may be found in recurrences and vice versa, so
that there would not appear to be any importance in
distinguishing between the two histological pictures,
unless they could be linked with a differing behaviour
or prognosis.

In this present study of 34 cases, therefore, we
have classified our cases according to the maximum
degree of differentiation attained by the tumour
throughout its course, in order that any factors of
clinical or prognostic value might thereby be
uncovered. The categories are as follows:
(a) Embryonal sarcomata, completely undifferenti-
ated; (b) non-striated embryonal rhabdomyo-
sarcoma, where rhabdomyoblasts may be recog-
ized but no cross-striations found; and (c) striated
embryonal rhabdomyosarcoma, where cross-
striations have been demonstrated at some stage.

In this series of 34 cases, there were 10 (29%)
embryonal sarcomata, six (18%) non-striated
embryonal rhabdomyosarcoma, and 18 (53%)
striated embryonal rhabdomyosarcoma. The
striated form of this neoplasm is thus the commonest.

The clinico-pathological details of the whole series
are briefly summarized in Tables I, II, and III, and
eight cases have been selected to illustrate the typical
features.

**EMBRYONAL SARCOMA**

**CASE 10** A male (A.B.), aged 6 years, presented
with proptosis of the right eye in April 1945. Excision of
an orbital tumour was followed by irradiation. The lesion
was diagnosed by the hospital pathologist as a fibro-
sarcoma. The sections of the tumour were first seen in
this department in April 1956 when the patient was being
examined at a follow-up clinic. They showed an embryonal
sarcoma consisting of primitive mesenchymal cells,
pleomorphism being a prominent feature. Some of
the cells had vesicular nuclei, and mitoses were common.
Rhabdomyoblasts, however, were not identified.

The patient was alive and well 19 years after onset with
no evidence of recurrence.

**CASE 30** A male (S.J.), aged 3 years, developed proptosis
of the left eye in June 1962 due to a tumour in the floor
of the orbit, extending into the apex. Excision of the
tumour was followed by irradiation.

**TABLE I**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Site of Presentation</th>
<th>Histology</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>12</td>
<td>M</td>
<td>(R) Orbit</td>
<td>Sheets of primitive mesenchymal cells</td>
<td>Excision of tumour</td>
<td>Untraced</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>M</td>
<td>(L) Upper Orbit</td>
<td>Sheets of primitive mesenchymal cells</td>
<td>(1) Excision of tumour</td>
<td>Died 9 months after onset</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>M</td>
<td>(R) Orbit</td>
<td>Tumour composed of primitive mesenchymal cells, showing marked pleomorphism</td>
<td>Excision of tumour, followed by irradiation</td>
<td>Alive and well 19 years after onset</td>
</tr>
<tr>
<td>16</td>
<td>17</td>
<td>M</td>
<td>(R) Upper lid</td>
<td>Encapsulated mass consisting of pleomorphic mesenchymal cells with numerous mitotic figures</td>
<td>(1) Excision</td>
<td>Died 10 months after onset; cerebral and pulmonary metastases</td>
</tr>
<tr>
<td>26</td>
<td>7</td>
<td>M</td>
<td>(R) Upper and inner orbit</td>
<td>Tumour consisted of mesenchymal cells and a few areas showing spindle cells</td>
<td>(1) Excision of tumour followed by irradiation</td>
<td>Untraced</td>
</tr>
<tr>
<td>28</td>
<td>7†</td>
<td>F</td>
<td>(L) Upper orbit</td>
<td>Sheets of primitive mesenchymal cells</td>
<td>Local excision of tumour</td>
<td>Died 7 months after onset</td>
</tr>
<tr>
<td>29</td>
<td>7</td>
<td>F</td>
<td>(R) Upper lid</td>
<td>Tumour consisted of primitive mesenchymal cells showing marked mitotic activity</td>
<td>Excision of tumour followed by irradiation</td>
<td>Alive and well 2 years after onset</td>
</tr>
<tr>
<td>30</td>
<td>3</td>
<td>M</td>
<td>Floor of (L) Orbit</td>
<td>Sheets of mesenchymal cells forming syncytial masses in places; a marked connective tissue reaction was present</td>
<td>Excision of tumour followed by irradiation</td>
<td>Alive 20 months after onset</td>
</tr>
<tr>
<td>31</td>
<td>4</td>
<td>F</td>
<td>Lateral part of (R) orbit</td>
<td>A vascular tumour consisting of primitive mesenchymal cells and showing partial differentiation towards connective tissue elements</td>
<td>Excision of tumour followed by irradiation</td>
<td>Alive and well one year after onset</td>
</tr>
<tr>
<td>34</td>
<td>4</td>
<td>M</td>
<td>(R) Upper lid</td>
<td>Tumour consisted of pleomorphic hyperchromatic cells arranged, in some areas, in alveolar nests</td>
<td>Excision of tumour and irradiation</td>
<td>Alive and well 3 months after onset</td>
</tr>
</tbody>
</table>

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*Norman Ashton and Gwyn Morgan*
### TABLE II

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Site of Presentation</th>
<th>Histology</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>2</td>
<td>M</td>
<td>(R) Lower lid</td>
<td>Grape-like tumour composed of mesenchymal cells, multinucleated giant cells and strap-like cells having eosinophilic cytoplasm</td>
<td>(1) Excision of tumour followed by irradiation (2) Exenteration and irradiation for orbital recurrence</td>
<td>Died 22 months after onset</td>
</tr>
<tr>
<td>14</td>
<td>7</td>
<td>M</td>
<td>(L) Orbit</td>
<td>Biopsy showed a tumour composed of sheets of round, ovoid and strap-like cells having eosinophilic cytoplasm</td>
<td>Exenteration (1 year later) followed by irradiation</td>
<td>Died 12 months after onset</td>
</tr>
<tr>
<td>18</td>
<td>17</td>
<td>M</td>
<td>(L) Orbit</td>
<td>The biopsy showed a tumour composed of oval shaped cells, spindle cells and some strap-like cells with eosinophilic cytoplasm</td>
<td>(1) Exenteration (2) Irradiation for orbital recurrence</td>
<td>Died 15 months after onset</td>
</tr>
<tr>
<td>19</td>
<td>13</td>
<td>M</td>
<td>(R) Inner canthus</td>
<td>Tumour showed a mixture of spindle cells and strap-like cells with eosinophilic cytoplasm</td>
<td>Excision of tumour followed by irradiation</td>
<td>Died 15 months after onset</td>
</tr>
<tr>
<td>24</td>
<td>3</td>
<td>F</td>
<td>(L) Inner and upper orbit</td>
<td>Pleomorphic collection of tumour cells, some showing eosinophilic cytoplasm; an alveolar arrangement present in places together with areas of vascularity and necrosis</td>
<td>(1) Exenteration and irradiation (2) Irradiation for lymph node enlargement</td>
<td>Alive and well after 38 months</td>
</tr>
<tr>
<td>25</td>
<td>8</td>
<td>F</td>
<td>(R) Upper and outer orbit</td>
<td>A malignant tumour showing a number of elongated cells with eosinophilic cytoplasm; the stroma showed a marked connective tissue reaction</td>
<td>Excision of tumour followed by irradiation</td>
<td>Untraced</td>
</tr>
</tbody>
</table>

Histological examination showed an embryonal sarcoma consisting of mesenchymal cells forming syncitial masses in places. The patient remained well until an orbital recurrence in February 1964 (20 months after onset), and exenteration of the orbit was performed.

**NON-STRIATED EMBRYONAL RHABDOMYOSARCOMA**

**CASE 14** A male (M.H.), aged 7 years, developed proptosis of the left eye due to an orbital tumour in June 1957.

Histological examination of a biopsy showed sheets of neoplastic cells, some round, others ovoid, and a few strap-like with eosinophilic cytoplasm. Cross-striations were not seen. Exenteration of the orbit was performed, followed by irradiation.

A recurrence of the orbital tumour, extending into the antrum, occurred in April 1958 and the patient died in June 1958, 12 months after the onset.

No post-mortem examination was performed.

**STRIATED EMBRYONAL RHABDOMYOSARCOMA**

**CASE 7** A male (F.A.), aged 6 years, presented in July 1955 with a small, reddish mass at the left inner canthus, which grew to the size of a pea in two weeks (Fig. 1). This was excised. Histological examination showed a myxomatous tumour (Fig. 2) consisting of round hyperchromatic cells tending to be arranged in rosettes, and a diagnosis of neuroblastoma was made. Local recurrence of the tumour was excised in September 1955, followed by irradiation. Histological examination showed a similar picture to the previous biopsy, but without rosette formation. A few giant cells were now present together with strap-like cells having abundant eosinophilic cytoplasm, i.e., rhabdomyoblasts. Cross-striations, however, were absent. The tumour was diagnosed as a non-striated rhabdomyosarcoma.

A metastasis developed in May 1956 in a preauricular lymph node; this responded to irradiation.

A recurrence in the floor of the orbit was exenterated in November 1956 (Fig. 3). Histological examination showed an anaplastic sarcoma.

There was an orbital recurrence in January 1957 (Fig. 4) and histological examination showed the same picture as previously.

The patient died in May 1957, 22 months after the onset.

Post-mortem examination showed tumour extension into the frontal and sphenoidal bones with destruction of the pituitary gland (Fig. 5). Metastases were present in the spine, sternum, pelvis, femur, and lungs. Cross-striations were demonstrated for the first time in the intracranial extension.

**CASE 9** A male (P.H.), aged 8 years, attended hospital in September 1955, with what appeared to be a chalazion of the left upper lid. This was incised and curretted. A recurrence at the previous site occurred in November 1955 (Fig. 6a).
<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Site of Presentation</th>
<th>Histology</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>F</td>
<td>(L) Orbit</td>
<td>Tumour showed a mixture of round, oval and strap-like cells with eosinophilic cytoplasm. Cross-striations present in some cells</td>
<td>(1) Excision of tumour (2) Excision of recurrences on 5 occasions (3) Exenteration for final recurrence</td>
<td>Died 4 years after onset</td>
</tr>
<tr>
<td>4</td>
<td>8/12</td>
<td>F</td>
<td>(L) Orbit</td>
<td>Hyperchromatic round and oval cells, and strap-like cells with eosinophilic cytoplasm, some cells with cross-striations</td>
<td>Excision of tumour</td>
<td>Untraced</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>F</td>
<td>(L) Lower lid</td>
<td>Tumour consisted of hyperchromatic round and polyhedral cells and large plasmoidal and spindle-shaped giant cells with abundant eosinophilic cytoplasm. Cross-striations present in some cells</td>
<td>(1) Biopsy and irradiation (2) Exenteration as tumour was resistant to irradiation</td>
<td>Died 6 months after onset with metastases in brain and lungs</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>F</td>
<td>(R) Upper lid</td>
<td>Syncytial sheets of pleomorphic mesenchymal cells showing numerous mitoses and related to thin-walled blood vessels Many strap-like cells with eosinophilic cytoplasm showing cross-striations</td>
<td>(1) Biopsy and irradiation (2) Exenteration followed by irradiation as tumour proved resistant to irradiation</td>
<td>Died 6 months after onset</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>M</td>
<td>(L) Inner canthus</td>
<td>Highly malignant myxomatous tumour composed of hyperchromatic cells showing some rosette formation (? neuroblastoma). Strap-like cells were seen in recurrences, and cross-striations were present in the metastatic deposits in the lungs</td>
<td>(1) Excision (2) Irradiation for recurrence (3) Excision for recurrence (5) Irradiation for lymph node metastasis (6) Exenteration for orbital recurrence</td>
<td>Died 22 months after onset with metastases in pre-auricular lymph node, lungs, and bones</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>M</td>
<td>(L) Orbit</td>
<td>Tumour composed of spindle cells and plasmoidal giant cells showing vacuolation and eosinophilic cytoplasm, some cells showing cross-striations. Stroma showed a marked connective tissue reaction</td>
<td>(1) Irradiation (2) Irradiation for recurrence was unsuccessful; excision of tumour (3) Irradiation for recurrence (4) Irradiation for further recurrence followed by exenteration</td>
<td>Died 17 months after onset with metastases in brain, trachea, and lungs</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>M</td>
<td>(L) Upper lid</td>
<td>A mixture of round, ovoid, spindle and strap-like cells, some having eosinophilic cytoplasm. There were many fusiform and ribbon-like cells, some with cross-striations. A large number of mature muscle cells were seen</td>
<td>(1) Excision (2) Irradiation for recurrence (3) Irradiation for lymph node recurrence</td>
<td>Alive and well 8⅔ years after onset</td>
</tr>
<tr>
<td>11</td>
<td>6½</td>
<td>F</td>
<td>(R) Lower lid</td>
<td>Tumour composed of strap-like and ribbon-like cells with granular eosinophilic cytoplasm. Cross-striations seen in cells in orbital recurrence and pulmonary metastases</td>
<td>(1) Excision of tumour followed by irradiation (2) Exenteration for orbital recurrence</td>
<td>Died 15 months after onset with metastases in lungs and diaphragm</td>
</tr>
<tr>
<td>13</td>
<td>4</td>
<td>F</td>
<td>(R) Lower lid</td>
<td>Tumour consisted of cells with eosinophilic cytoplasm, many being giant cells. Cross-striations were present in some of the cells</td>
<td>(1) Excision of tumour (2) Irradiation for recurrence unsuccessful (3) Exenteration</td>
<td>Alive and well 7 years after onset</td>
</tr>
</tbody>
</table>
### Table III continued

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Site of Presentation</th>
<th>Histology</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>12</td>
<td>F</td>
<td>(R) Lower lid</td>
<td>Tumour consisted of hyperchromatic spindle, polyhedral, and giant cells, some showing cross-striations</td>
<td>(1) Biopsy followed by exenteration and irradiation</td>
<td>Died 15 months after onset</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2) Irradiation for orbital recurrence</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>9</td>
<td>M</td>
<td>(R) Upper lid</td>
<td>Encapsulated tumour showed fascicular bundles of pleomorphic cells, some being round and others oval and strap-like with eosinophilic cytoplasm. Cross-striations were present in some of the cells</td>
<td>Excision of tumour followed by exenteration</td>
<td>Alive and well 5 years after onset</td>
</tr>
<tr>
<td>20</td>
<td>4½</td>
<td>F</td>
<td>(R) Upper fornix</td>
<td>Encapsulated tumour composed of sheets of pleomorphic, hyperchromatic cells with many mitoses. Some strap-like cells showing cross-striations were present. The stroma showed a marked connective tissue reaction</td>
<td>(1) Excision of tumour</td>
<td>Alive and well 50 months after onset</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2) Exenteration</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(3) Irradiation for lymph node metastasis</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>5</td>
<td>F</td>
<td>(R) Lacrimal gland region</td>
<td>Tumour composed of mesenchymal cells and strap-like cells with eosinophilic cytoplasm, some of the latter showing scanty cross-striations</td>
<td>Biopsy of tumour followed by exenteration</td>
<td>Died 12 months after onset</td>
</tr>
<tr>
<td>22</td>
<td>10</td>
<td>M</td>
<td>(R) Orbit upper and medial aspects</td>
<td>Mass consisted of round and elongated cells, a few with eosinophilic cytoplasm showing cross-striations. A stromal connective tissue reaction resulting in a similar appearance, in places, to the alveolar type of tumour</td>
<td>(1) Excision of mass followed by irradiation</td>
<td>Died 19 months after onset</td>
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<td></td>
<td></td>
<td>(2) Irradiation for orbital recurrence</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td>(3) Further irradiation for orbital recurrence</td>
<td></td>
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<tr>
<td>27</td>
<td>6</td>
<td>M</td>
<td>(L) Orbit</td>
<td>Tumour showed sheets of hyperchromatic mesenchymal cells with a scanty fibrovascular stroma. Marked pleomorphism was seen and occasional strap-like cells with cross-striations were present</td>
<td>Exenteration or orbit</td>
<td>Untraced</td>
</tr>
<tr>
<td>32</td>
<td>14</td>
<td>F</td>
<td>(R) Lower and outer orbit</td>
<td>Primitive mesenchymal cells in a vascular stroma were seen. Cells with eosinophilic cytoplasm and strap-like cells were common and occasional cross-striations were present</td>
<td>(1) Biopsy followed by excision and irradiation</td>
<td>Alive and well 30 months after onset</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>(2) Exenteration for orbital recurrence</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>3</td>
<td>M</td>
<td>(R) Upper lid</td>
<td>Tumour showed sheets of ovoid and strap-like cells with eosinophilic cytoplasm, some with scanty cross-striations</td>
<td>(1) Biopsy, partial excision of tumour and irradiation</td>
<td>Alive and well 3 months after onset</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>(2) Exenteration as tumour proved to be radio-resistant</td>
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</table>
Case 7. A small reddish mass situated at the left inner canthus grew to the size of a pea in two weeks. It was excised.

FIG. 2. Case 7. Biopsy of lesion in Fig. 1, showing undifferentiated embryonal sarcoma.

FIG. 3. Case 7. One year after onset. Recurrence in floor of orbit after a course of irradiation. This was treated by exenteration.


FIG. 5. Case 7. Open skull at necropsy showing extension into left sphenoidal bone and invasion of pituitary (arrow). Cross striations were demonstrated for first time in the rhabdomyoblasts of intracranial extensions.
Embryonal sarcoma and embryonal rhabdomyosarcoma of the orbit

Fig. 6a, b, and c. Case 9. (a) recurrence in left upper lid of a ? chalazion removed two months previously. This was excised and showed striated embryonal rhabdomyosarcoma. cf. Figs. 7 and 8. (b) Second recurrence at inner canthus. (c) Successfully irradiated.

Fig. 7. Case 9. The growth consisted of round, ovoid, spindle, and strap-like cells with abundant eosinophilic cytoplasm. Haematoxylin and eosin × 200.

The recurrence enlarged and was widely excised in January 1956.

Histological examination showed two polypoidal masses consisting of round, ovoid, spindle, and strap-like cells, the latter having abundant, eosinophilic cytoplasm. Cross-striations were present and many of the cells resembled mature muscle fibres (Figs. 7 and 8).

There was a recurrence in the orbit (Fig. 6b) which responded to irradiation (Fig. 6c).

Fig. 8. High-power view of Fig. 7 showing cross-striations in a rhabdomyoblast. × 1,250.

A metastasis in a pre-auricular lymph node occurred in May 1959, and histological examination showed a similar picture; the lymph node responded to irradiation.

The patient was alive and well eight and a half years after the onset, with no further recurrence.

Case 11 A female (S.W.), aged 6½ years, developed a swelling under the right lower lid (Figs. 9 and 10) in December 1955. This was locally excised. Histological
FIGS. 9 and 10. Case 11. Front and side views of a tumour in the right lower lid. This was excised and histology showed a non-striated embryonal rhabdomyosarcoma.

FIG. 11. Case 11. Despite excision and irradiation recurrence occurred six months later and exenteration was performed.

FIG. 12. Case 11. Recurrence in exenterated orbit after three months. Patient died with metastases 15 months after onset. Cross striations found in metastases.

examination showed a malignant tumour with numerous strap-like rhabdomyoblasts. Cross-striations were not seen. A course of irradiation was given, but in June 1956 exenteration of the orbit was carried out following an orbital recurrence (Fig. 11). The histological picture was similar to that previously seen.

A recurrence in the exenterated orbit was observed in September, 1956 (Fig. 12) and the patient died in February 1957, 15 months after the onset.

Post-mortem examination showed metastases in the lungs and diaphragm, and striated rhabdomyoblasts were present in the orbital tumour and lung metastases.
CASE 20  A female (A.K.), aged 4½ years, presented with a small red polyp in the right upper fornix in November 1959.

Histological examination of the mass revealed sheets of neoplastic cells with hyperchromatic nuclei, marked pleomorphism, and many mitoses (Fig. 13). Many of the cells had abundant eosinophilic cytoplasm, and some were pear-shaped or strap-shaped (Fig. 14). Cross-striations were demonstrated.

During the period February 1960 and January 1961, exenteration of the orbit was performed in Sweden. A metastasis in a lymph node in the region of the right parotid gland was treated by irradiation in November 1961, and in May 1962 the lymph node appeared reduced in size. A further lymph node was noted at the angle of the right jaw in September, 1962, but the patient was alive and well, without recurrence, in August 1964, 57 months after the onset.

CASE 33  A male (D.N.), aged 3 years, complained of a swelling of the right upper lid for two weeks apparently precipitated by a blow (Figs. 15 and 16). The eye was proptosed downwards, and the lower palpebral conjunctiva was exposed. A biopsy was performed. The histological picture showed a mixture of primitive mesenchymal cells and rhabdomyoblasts; scanty cross-striations were demonstrated.

Irradiation was unsuccessful, the tumour gradually increasing in size, and in June 1964 exenteration of the orbit was carried out. The patient was alive and well in July 1964, five months after the onset.

Electron microscopical examination of the tumour showed actomyosin filaments in the cytoplasm of the neoplastic cells (Fig. 17). Both thick and thin actomyosin filaments were seen, the former measuring approximately 150 Å units and the latter 50 Å units in width. Ribonucleoprotein particles, normally present in cells engaged in protein synthesis, were found in close association with these filaments, and it seems reasonable to assume that they are engaged in the synthesis of actomyosin. Kroll, Kuwabara, and Howard (1963) examined two cases of rhabdomyosarcoma electron microscopically and demonstrated similar actomyosin filaments in one of the tumours which had shown cross-striations when examined by the light microscope. Actomyosin filaments were not seen, however, under the electron microscope in the other tumour which was a non-striated rhabdomyosarcoma. Friedman, Harrison, Tucker, and Bird (1965) demonstrated actomyosin filaments in a rhabdomyosarcoma of the ear.

**FINDINGS AND DISCUSSION**

**AGE**  It will be seen from Tables I, II, and III, and Fig. 18 that the age of onset ranged between 2 months and 17 years, the peak incidence falling between 3 and 8 years and the average was 7-2 years, a figure which accords closely with that of Reese (1951), 7 years, and that of Porterfield and Zimmerman (1962), 8 years.

FIG. 17. Electron micrograph of tumour showing actomyosin filaments (arrows) in the cytoplasm of the neoplastic cells. × 22,400.
Embryonal sarcoma and embryonal rhabdomyosarcoma of the orbit

Of the 34 patients in the series 19 were males (55.8%) and 15 were females (44.2%). This incidence also accords fairly closely with that of Porterfield and Zimmerman (1962), in whose series 65% of 55 cases were males, but differs from that of Reese (1951) who has stated that orbital rhabdomyosarcoma occurs twice as frequently in males.

LOCATION The right side was more frequently involved than the left (R 20: L 14), but there was no special tendency for the upper and inner portions of the orbit to be involved as in the cases of Reese and Calhoun (1941) and Porterfield and Zimmerman (1962). In none of the 34 cases in the series was there any evidence of the neoplasm having originated in the extraocular muscles. The localization of the tumours is summarized in Table IV.

### TABLE IV

<table>
<thead>
<tr>
<th>Site of Presentation</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>(L) Orbit</td>
<td>11</td>
</tr>
<tr>
<td>(R) Orbit</td>
<td>7</td>
</tr>
<tr>
<td>(L) Upper lid</td>
<td>1</td>
</tr>
<tr>
<td>(R) Upper lid</td>
<td>6</td>
</tr>
<tr>
<td>(L) Lower lid</td>
<td>1</td>
</tr>
<tr>
<td>(R) Lower lid</td>
<td>4</td>
</tr>
<tr>
<td>(L) Inner canthus</td>
<td>1</td>
</tr>
<tr>
<td>(R) Inner canthus</td>
<td>1</td>
</tr>
<tr>
<td>(R) Lacrimal gland region</td>
<td>1</td>
</tr>
</tbody>
</table>

**HISTOPATHOLOGY** Three of the tumours were encapsulated, a feature which was not related to the eventual outcome. The histological picture as seen in the 34 cases was remarkably diverse, including primitive mesenchymal cells, hyperchromatic round and pleomorphic cells, bizarre vacuolated giant cells, strap or ribbon-shaped cells and tadpole-shaped cells, with abundant eosinophilic cytoplasm (with or without cross striations), and in one case relatively well-formed muscle fibres (Figs. 19-24). In contrast with most malignant tumours, these growths may differentiate as the case progresses. This is well illustrated in case 7 where cross-striations were absent in the primary and recurrent growths, but were apparent at post-mortem examination. The stroma, which may show non-specific mucoid degenerative changes, is sometimes excessive in amount (cases 8, 20, 25, and 30).

In 1956 Riopelle and Thériault described a form of rhabdomyosarcoma consisting of an interlacing framework of connective tissue surrounding groups of tumour cells, some of which adhere to the septa while others lie loosely in the spaces, and they named it ‘alveolar rhabdomyosarcoma’. In a study of 170 cases of rhabdomyosarcoma of the head and neck by Dito and Batsakis (1962) four were classified as alveolar (2.4%), whereas in the series of orbital cases described by Porterfield and Zimmerman (1962) 14% were of this type, with a tendency to be located in the lower part of the orbit and to carry a

FIG. 20. Area typical of non-striated rhabdomyosarcoma showing strap-shaped and tadpole-shaped rhabdomyoblasts with abundant non-striated eosinophilic cytoplasm. Haematoxylin and eosin × 625.


FIG. 22. Another area of section in Fig. 21, showing a central striated rhabdomyoblast. × 1,100.
Embryonal sarcoma and embryonal rhabdomyosarcoma of the orbit

FIG. 23. Case 13. Area from a striated rhabdomyosarcoma showing a highly pleomorphic picture with some multinucleated cells. Haematoxylin and eosin × 625.

FIG. 24. Case 8. Area from a striated rhabdomyosarcoma showing vacuolated giant cells. Haematoxylin and eosin × 1,200.


FIG. 26. High-power view of Fig. 24 showing fibrovascular framework containing groups of tumour cells some of which adhere to the septa and others lie loosely in the spaces. Haematoxylin and eosin × 170.
particularly poor prognosis; only one patient survived for more than two years. In our own series only three cases (cases 22, 24, and 34) presented this alveolar pattern (9%), and then in only some areas of the growth (Figs. 25 and 26). This group contained one case from each of our three histological categories. In contrast to the cases of Porterfield and Zimmerman (1962) they were all from the upper lid or upper orbit. One patient died (case 22) 19 months after onset, and the other patients are still alive, one (case 24) having survived over three years. It is our impression that the alveolar form, although presenting a well-defined pattern, is merely due to a stromal reaction which may develop in any part and at any stage of a rhabdomyosarcoma and we rather doubt whether its allocation to a special category is useful or justifiable.

Treatment is analysed in Table V. The commonest forms of treatment were excision followed by exenteration and irradiation, and excision followed by irradiation. The general methods of radiotherapy involved the external application of high energy sources or the implantation of radioactive materials emitting gamma rays (radium needles or tantalum wire). The dosage was usually in the region of 5,000 rads over a period of five to eight weeks. Case 18 (Table II) was treated in addition by an antimitabolite, Methotrexate, instilled into the right internal carotid artery in daily doses of 15 mg. to a total dose of 162.5 mg. An alkylating agent, Cyclophosphamide, was administered to case 32 (Table III) by carotid infusion in doses of 40 mg. per kilogram of body weight per day.

**TABLE V**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Embryonal Sarcoma (10)</th>
<th>Non-striated Embryonal rhabdomyosarcoma (6)</th>
<th>Striated Embryonal rhabdomyosarcoma (18)</th>
<th>Total (34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excision alone</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Excision and irradiation</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Excision and exenteration</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Excision, exenteration, and irradiation</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Exenteration</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Exenteration and irradiation</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Irradiation alone</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**FOLLOW-UP** It is known that the prognosis of rhabdomyosarcoma in the head and neck is extremely poor (Patton and Horn, 1962; Koop and Tewarson, 1964) although it has been reported to be somewhat better in the orbital cases (Dito and Batsakis, 1962).

Of the 34 patients in our series five were untraced; of the remaining 29 patients, 16 have died of the tumour, five are living having had a local recurrence, and eight are alive without recurrence (Table VI).

**TIME OF DEATH** Of the 16 patients who died, 15 did so within 22 months of the onset of symptoms and only one (case 1) survived longer (54 months); the majority (11) died within 15 months (Fig. 27).
The prognosis of patients surviving beyond two years without recurrence is therefore excellent.

RECURRENTS AND METASTASES Orbital recurrence occurring within 20 months of onset was seen in 21 of 29 patients, and, as to be expected, it was a bad prognostic feature for 15 of these patients died in less than two years and one within four and a half years of the appearance of the primary lesion. Five patients died with metastases, the lungs being the most commonly affected organ, a finding in accord with that of Frayer and Enterline (1959). On the other hand, neither recurrence nor metastases were necessarily fatal; cases 9 and 13 have survived eight and a half and seven years respectively after local recurrence, while cases 9 and 20 have survived metastases in pre-auricular lymph nodes.

LONG SURVIVAL The fate of 22 cases after a period of three years or more is known; of these, seven survived, giving a three-year survival rate of 32%, which may be compared with 47% quoted by Reese (1963) in a series of 44 cases. The fate of 20 cases after a period of five years is known; of these only four have survived, giving a five-year survival rate of 20%, which is better than the five-year survival rate of head and neck tumours as a whole (8-2%; Dito and Batsakis, 1962). Of the four surviving patients, one is alive after 19 years, one after eight and a half years, one after seven years, and one after five years (Table VII).

TABLE VII
FOUR CASES SURVIVING OVER 5 YEARS

<table>
<thead>
<tr>
<th>Case</th>
<th>Survival</th>
<th>Histology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 R.W. 4079/59</td>
<td>5 years</td>
<td>Striated rhabdomyosarcoma</td>
<td>(1) Excision (2) Exenteration</td>
</tr>
<tr>
<td>13 M.T. 7107/57</td>
<td>7 years</td>
<td>Striated rhabdomyosarcoma</td>
<td>(1) Excision (2) Excision for recurrence (3) Irradiation for recurrence (4) Exenteration</td>
</tr>
<tr>
<td>9 P.H. 3118/56</td>
<td>8½ years</td>
<td>Striated rhabdomyosarcoma</td>
<td>(1) Excision (2) Irradiation for recurrence (3) Irradiation of lymph node (4) + Excision node</td>
</tr>
<tr>
<td>10 M.B. 10722/56</td>
<td>19 years</td>
<td>Embryonal sarcoma</td>
<td>(1) Excision (2) Irradiation</td>
</tr>
</tbody>
</table>

SURVIVAL AND HISTOLOGICAL TYPE Of the three histological categories of embryonal sarcoma, non-striated embryonal rhabdomyosarcoma, and striated embryonal rhabdomyosarcoma, the respective survival rates for three years were 25% (one of four), 20% (one of five) and 38% (five of 13), suggesting a slightly better prognosis for the most differentiated tumours, as was found by Porterfield and Zimmerman (1962) in their series of cases. This was not borne out by the five-year survival rates, however, which were 25% (one of four), 0% (none of four), and 25% (three of 12). Our experience, therefore, provides no evidence that the histological category materially influences the ultimate outcome.

SURVIVAL AND TREATMENT The inadequacy of modern treatment of these tumours is shown by the high death rate in the present series (80% after five years), wherein many different combinations of therapy had been tried. Nor can the successful outcome in our long-term survivals be attributed to any particular line of treatment (Table VII). For instance, early exenteration of these tumours has been strongly advocated as the treatment of choice (Porterfield and Zimmerman, 1962; Reese, 1963), but of our four long-term survivors (five years or over) early exenteration was performed in only one (case 17), while the two longest survivors were treated by simple excision followed by irradiation (cases 9 and 10). In the whole series the five-year survival rate for primary excision (with or without irradiation) was 25%, and for primary exenteration (with or without irradiation) was 14%. We therefore agree with Lederman (1956) that at the present time there is no conclusive evidence to show that immediate exenteration is advantageous.

It has been stated that these tumours are radio-resistant, whether extra-orbital (Geschickter, 1934; Rakov, 1937; or intra-orbital (Reese and Calhoun, 1941; Reese, 1951; Offret, 1951), and it seems that this opinion is substantially true for in at least eight of the cases in this series (cases 6, 8, 12, 13, 15, 16, 18, and 19) irradiation was ineffective. Nevertheless, although rarely radiocurable, they may be highly radiosensitive initially, and Lederman (1956) advocates that radiotherapy should always be used in the first instance and it may be of value in controlling recurrences, as in our cases 9, 20 (apparently cured) and case 26 (untraced). These encouraging reactions, however, have little influence on the ultimate outcome. In the series of 55 cases of Porterfield and Zimmerman (1962) not one of the patients whose primary treatment was irradiation survived longer than three years. Only one of our cases (case 8) was treated primarily with irradiation, and he died within 17 months.

We can refer only briefly to the efficacy of chemotherapy, for our follow-up includes only two cases treated in this way. Some success with actinomycin D alone and in combination with x-ray therapy has been reported (Farber, Toch, Sears, and Pinkel, 1956; Pinkel, 1959; Tan, Dargeon, and Burchenal, 1959), and Koop and Tewarson (1964) advocate the combination of aggressive surgery, intra-arterial
infusion of an anticancer drug during the procedure, and post-operative anticancer chemotherapy as the best treatment in the present state of our knowledge. As previously stated under the section describing the forms of treatment in this series, case 18 was treated by daily intracarotid infusions of the antimetabolite Methotrexate and case 32 by carotid infusion of the alkylating agent Cyclophosphamide; in both cases this was in addition to irradiation. Case 18 died within 15 months, and although case 32 is alive nine months after onset, chemotherapy did not prevent the need for exenteration. In neither case, therefore, was treatment successful. Further experience with this treatment, however, is required, but from the present study it would appear that initial excision followed by irradiation, with exenteration held in reserve for recurrences and radio-resistant cases, was a somewhat more satisfactory procedure than any other course of treatment.

It is a pleasure to acknowledge the kind co-operation of the many clinicians concerned in the follow-up inquiry for without their help this survey would clearly have been impossible. Our thanks are especially due to Mr. G. Knight, Mr. D. Wood, Miss E. Fitzgerald, and Mrs. E. Hond for help with the considerable correspondence and analysis of figures.

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Norman Ashton and Gwyn Morgan

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