THE SEX RATIO IN CONVULSIVE DISORDERS
WITH A NOTE ON SINGLE-SEX SIBSHIPS

BY

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In many, and perhaps indeed in the majority of diseases, one sex tends to be affected more often than the other, and the convulsive disorders of children appear to provide an example of such a differential sex incidence.

Lennox, Gibbs, and Gibbs (1940) in a series of more than 2,000 cases, found that 57% of their affected patients were male and 43% female. Lennox (1949), in a series of over 150 children with febrile convulsive disorders found a ratio of 62% males to 38% females, and she concluded that maleness was an aetiological factor to be given weight comparable with that of age, heredity, and degree of fever. This conclusion, if valid, is clearly of importance in the natural history of the syndrome and of general biological interest.

In this paper we present an analysis based on a personal series of children with fits. The sex ratio we found was very like that of other workers, but on the general principle that any biological variation should be compared with that in a control group, we also studied the sex ratio in the unaffected siblings of our patients. The results obtained by this method seem to cast doubt on the validity of employing the sex ratio as a measure of the aetiological weight of sex in this or in other diseases. Our enquiry also showed a possible relationship between the hereditary factor in convulsive disorders and the sex ratio, both in the affected children and in their brothers and sisters.

Sources

This study is part of a larger study of the natural history of convulsive disorders in childhood. The study began on November 1, 1949, and still continues. The patients were drawn from the following sources:—

Hospital In-Patients.—Every child with a convulsive disorder admitted to the wards of the children’s departments of the Radcliffe Infirmary and Churchill Hospital, Oxford, was seen by me on admission, and followed through in the Out-patient Department after discharge from hospital. Any child who developed convulsive seizures after admission was similarly treated.

Hospital Out-Patients.—Every child referred to the Paediatric Out-Patient Department with a convulsive disorder after seeing the consultant paediatrician was seen by me and was followed up.

Patients Reported by Health Visitors.—The Medical Officer of Health for Oxford allowed me to arrange a simple scheme by which health visitors in their routine visits notified any child whose mother gave a history that the child had had a convulsion. I then visited the children in their homes. The health visitors specifically enquired about convulsions at each visit. They cover roughly 85% of all the children in Oxford under the age of 4 years.

The Mothercraft Clinic.—This voluntary, fee-paying organization has a membership largely drawn from middle-class people, who often do not attend the city clinics. The sister in charge notified any child who had a convulsion and I then visited the family.

Infant Welfare Clinics.—These municipal clinics referred some affected children to the hospital Out-patient Department, and they then entered the study via the consultant paediatrician.

The first sample analysed in this pilot survey consists of the family trees of 200 children, forming a consecutive series of those seen between January 7, 1950, and November 18, 1950. This sample is probably a fair cross-section of the convulsive disorders of children as they present in Oxford at the present time.

It is of importance to note that no selection was made on the aetiology of the seizures, for no exact method is available for distinguishing so-called
idio
tic epi
ty from other types of seizure in
children. The occurrence of some sort of convulsive

disorder was the sole condition of entry to the
sample. The term "convulsive disorders" is used
to cover all the recognized convulsive syndromes,
e.g., idiopathic epilepsy, acquired epilepsy, febrile

cou
vulsions etc., and the term "fit" covers all
types of individual seizure, e.g., generalized, grand
mal, minor motor seizure, focal seizure, petit mal,
etc. Syncope was excluded.

The age range in this sample was from 1 day to
12 years at entry.

**Drawing the Family Tree**

A careful enquiry for a history of convulsive
disorders among blood-relations was made in every
case. Questioning of this kind was found to be a
matter of some delicacy. It was my practice to
delay the making of a tree until the mother's first
fright had subsided, and until her friendship had
been gained. It was then explained that a know-
ledge of the family background was a help in the

treatment of the child, and the mother was asked to
enquire of the child's grandparents, aunts, and
uncles for any case of epilepsy or convulsions of
any kind.

A history was accepted as positive if a clear
history of a genuine fit was obtained: where doubt
existed about the nature of the attack that relative
was excluded.

The only relations considered in this analysis are
full siblings, parents, aunts and uncles, and grand-
parents of the propositus.

**Analysis of the Present Sample**

Examination of our sample of 200 children
showed a ratio close to that given by Lennox,
Gibbs, and Gibbs (1940) and by Lennox (1949).
Of our patients 118 (59%) were male and 82
(41%) were female. The ratio held good whether
the diagnosis was "epilepsy" or "convulsions".

Of those diagnosed as "convulsions", 59.1% were
male, and of the "epileptics" 57.9% were male.

On the absolute figures the small percentage
difference was not of statistical significance.

At first sight this appeared to confirm a selective
incidence. When, however, the siblings of the
affected children were divided into males and
females, a favouring of males again was found: 156
males to 121 females or 56.3 and 43.7%. Of
these siblings, 34 had seizures and when these
children were divided into males and females and
added to the number of the propositus, two large
groups emerged, 234 children with seizures and
their 243 siblings without seizures (Table I).

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children with seizures</td>
<td>134</td>
<td>100</td>
<td>234</td>
</tr>
<tr>
<td>All normal siblings</td>
<td>140</td>
<td>103</td>
<td>243</td>
</tr>
<tr>
<td>Totals</td>
<td>274</td>
<td>203</td>
<td>477</td>
</tr>
</tbody>
</table>

In the group with seizures 57.3% were male, in
the group without seizures 57.6% were male. Thus
the incidence of males was the same in both groups.
Again, of the 477 children, 274 were males, and
of these males 48.9% had fits. There were 203
females, and of these females 49.3% had fits.
There is, in fact, homogeneity with regard to sex.
The sex ratio in the affected siblings (Table II) was
16 males to 18 females.

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>Male %</th>
<th>Female %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propositus</td>
<td>200</td>
<td>82</td>
<td>59</td>
<td>41</td>
</tr>
<tr>
<td>All siblings</td>
<td>277</td>
<td>121</td>
<td>56.3</td>
<td>43.7</td>
</tr>
<tr>
<td>Siblings with seizures</td>
<td>34</td>
<td>18</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>All children</td>
<td>477</td>
<td>203</td>
<td>57.4</td>
<td>42.6</td>
</tr>
<tr>
<td>All with seizures</td>
<td>234</td>
<td>100</td>
<td>56.9</td>
<td>43.1</td>
</tr>
<tr>
<td>All without seizures</td>
<td>243</td>
<td>103</td>
<td>57.9</td>
<td>42.1</td>
</tr>
<tr>
<td>Propositus &quot;epilepsy&quot;</td>
<td>112</td>
<td>45</td>
<td>59.1</td>
<td>40.9</td>
</tr>
</tbody>
</table>

When the sex ratio of affected children is then com-
pared with that of their unaffected siblings it
appears that, within families which manifest
seizures, sex is not a significant aetiological factor.

**Preponderance of Males**

The fact remains, however, that this series accords
with that of Lennox, Gibbs, and Gibbs in finding a
marked preponderance of males among affected
children of the order of 57 to 59%.

Gowers (1901), in a series of more than 3,000
patients with fits, found that 48% were male. So
it might appear that the sex ratio has changed in
the last 50 years. Plainly the most simple ex-
planation would be in the known change in this
period in the infant mortality rate. Male live
births preponderate over female, and male infant
mortality over female, hence a falling infant mor-
tality rate is likely to increase the number of young males in a given population, and in any sub-group of that population. Is the explanation then that there was in the population from which our sample was drawn an overall preponderance of males, at the seizure age, of the order of 58%? Critical examination suggests that this hypothesis also is invalid.

The Royal Commission on Population (1949) reported that the ratio of male to female live births in England and Wales varied little from 105 to 100. From birth onwards the females gain over the males, giving by adolescence a preponderance of females. This trend has recently altered and the excess of females is rapidly disappearing. The birth ratio, however, remains constant at 105 to 100; Myers (1949) reports that a similar ratio is constant in the U.S.A. Clearly the ratio in this series of 274 males to 203 females (that is 134 males per 100 females) markedly exceeds even the normal ratio at birth.

Sources of Error in the Analysis.—At the time this series was made the families of our patients could not, of course, be considered to be complete, although in fact these families had an average size of 2-4 children, a figure above the probable national average of completed families, which is roughly 2-2 at present (Report of Royal Commission on Population, 1949).* It is also to be expected that a number of siblings will at some future date develop convulsive seizures. Clearly final figures require a sample followed for 25 years.

There appears then to be a tendency to bear an unusually high proportion of surviving males in families of children afflicted with convulsive seizures. Within the group, however, the sex of a child does not affect its chance of developing a convulsive syndrome.

Tendency to Maleness Related to Family History of Fits

It seems to be unlikely that the sex of a child is a true aetiological factor. But we have shown that there is a tendency for families in which fits occur to contain an excess of males. Now if this tendency to bear sons were genetically associated with a tendency to fits, then the families of those affected children who have a family history of fits among close relatives might show an increased tendency to

* Comparison of family size between a series of this kind and the whole population will "normally" show larger families in the group studied, since these families must necessarily contain at least one living child.

maleness. This point may be examined in our series.

A family history was considered positive when the propositus had a sibling, parent, aunt, uncle, or grandparent who had a clear history of a convulsive disorder. The family history was positive in 75 cases in this series and negative in 125. Tables III, IV, and V set out the figures for the two groups.

**Table III**

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history positive (all children)</td>
<td>99</td>
<td>94</td>
<td>193</td>
</tr>
<tr>
<td>Family history negative (all children)</td>
<td>175</td>
<td>109</td>
<td>284</td>
</tr>
<tr>
<td>Totals</td>
<td>274</td>
<td>203</td>
<td>477</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 4.693 \]

**Table IV**

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propositus</td>
<td>40</td>
<td>35</td>
<td>75</td>
</tr>
<tr>
<td>Affected siblings</td>
<td>16</td>
<td>18</td>
<td>34</td>
</tr>
<tr>
<td>All affected</td>
<td>56</td>
<td>53</td>
<td>109</td>
</tr>
<tr>
<td>All unaffected</td>
<td>43</td>
<td>41</td>
<td>84</td>
</tr>
<tr>
<td>Totals</td>
<td>99</td>
<td>94</td>
<td>193</td>
</tr>
</tbody>
</table>

**Table V**

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propositus</td>
<td>72</td>
<td>47</td>
<td>125</td>
</tr>
<tr>
<td>Unaffected siblings</td>
<td>97</td>
<td>62</td>
<td>159</td>
</tr>
<tr>
<td>Totals</td>
<td>175</td>
<td>109</td>
<td>284</td>
</tr>
</tbody>
</table>

An unexpected fact emerges. The group with the negative family history contains the entire excess of males.

This is the exact converse of the expected finding. The Chi square suggests that our figures are statistically significant. The ratios hold good if the propositi are removed from each cell in Table III.

Now in the group with a positive history, as in the whole series, there is homogeneity with regard to sex; of all females, 56-4% had fits, and of all males, 56-6% had fits. The overall ratio of males to females is 105-3 males per 100 females, a ratio extremely close to the normal ratio of all live births. The ratio found when the propositi are excluded is exactly 100 males per 100 females (59 male siblings and 59 female siblings).
Where the family history was negative, there the sex ratio deviated grossly to 160·5 males per 100 females.

In spite of this fact, the sex of the child again did not appear to affect its chance of having a fit. Of all females in the negative family-history group, 56% had seizures; of all males in the same group, 55% had seizures. The percentage of each sex affected is, therefore, the same whether the family history is positive or negative and whether the tendency to maleness is present or absent.

We appear to have shown then that there is in children with convolutional disorders an association between a tendency to maleness in their families and an absence of seizures among close relatives.

**Relationship between “Epilepsy” and “Convolusions” in Negative Family History Group**

We have shown that the families of affected children with a negative family history contain an excess of males of the order 160 males per 100 females. Now this might be due to the fact that the group with a negative family history included as a subgroup some particular form of epileptic disease in which the maleness tendency was marked and the tendency to a familial incidence of seizures was absent. Inspection of the family trees suggested that this is unlikely to be true. The matter may, however, be tested a little more precisely.

Those propositi whose diagnosis was “convulsions” formed a relatively homogeneous clinical group. They were in general children who, with fever, below the age of 4 years, produced one or two isolated grand mal seizures without evidence of permanent cerebral damage. Families of the propositi from this group may then be compared with families from the more clinically mixed “epileptic” group, both groups being, of course, those in which a family history of seizures is absent.

Table VI shows, however, that the excess of males was in fact distributed evenly between the “convulsions” group and the “epilepsy” group. In the “convulsions” group 60.8% were males; in the “epilepsy” group 62.7% were males. The small percentage difference is not significant. Chi square is 0.082 on Table VI.

It appears that the tendency to maleness is a general property of the group with a negative family history.

I am unable to think of any simple genetic explanation that satisfies the facts given in this section. The findings do, however, serve to underline the essential unity of the convulsive disorders. With regard to the presence or absence of the family tendency to seizures and of the familial tendency to bear sons, the “epilepsy” and the “convulsion” groups appear to behave in an identical way.

**Single-sex Sibships**

The findings of this pilot survey seemed to be of rather general interest. The existence of families with a tendency to bear children all of one sex has long been suspected by geneticists, but no large group of such families has yet been isolated (Myers, 1949). The material collected in the present series offers an opportunity for isolating such a group. By attempting to do so we test also the suggestion made in the previous sections that a true tendency to bear an excess of males exists in the group studied, and that this tendency is limited to the sub-group with the negative family history.

For our hypothesis to be confirmed the following four propositions must be satisfied: (1) Incidence of all-male sibships in the group with a positive family history—within normal limits; (2) incidences of all-female and of mixed sibships in the same group—within normal limits; (3) incidence of all-male sibships in the group with a negative family history—a significant excess; (4) incidences of all-female and of mixed sibships in the same group—a corresponding reduction, which affects both the all-female and the mixed sibships to approximately the same degree.

**Methods.**—The statistical method evolved is a very simple comparison of observed and expected numbers in each size of sibship.

The reasoning proceeds thus. The ratio of male to female children at birth is 0.514 to 0.486, and this ratio is not greatly affected by maternal age or size of sibship (Lancaster, 1950). The ratio is applied here, and we make the assumption, therefore, that the overall ratio in the age-group from which our series is drawn does not differ significantly from the birth ratio. (This assumption is allowable, for we know that any difference there may be will be in favour of the females, hence any bias introduced will be against our hypothesis.)
Let \( S \) be the size of the sibship; let \( N_s \) be the number of sibships of size \( S \); let \( E_m \) be the expected number of sibships of size \( S \), that are composed entirely of boys; let \( p = 0.514 \).

Then

\[
E_m = N_s (0.514)^S \quad \ldots \ldots . \quad 1
\]

The variance of \( E_m \) for a sibship of size \( S \) is given by

\[
\text{Var} = N_s p (1 - p)^S \quad \ldots \ldots \quad 2
\]

The difference between observed (Ns) and expected (Em) may be calculated for each size of sibship, and the columns added up over the whole table. The excess of all-male-sibships is then given by

\[
\Sigma N_m - \Sigma E_m \quad \ldots \ldots \quad 3
\]

and the standard error (S.E.) is expressed by the sum of the variance \( \Sigma (\text{Var}) \). In order to establish that, for example, a significant excess of all-male-sibships is present in any subgroup it must be shown that:

\[
(\Sigma N_m - \Sigma E_m) \text{ is greater than, say, } 3 \ldots 4
\]

\[
\sqrt{\Sigma \text{(Var)}}
\]

When the figures are arrayed in this way allowance is made for the number of sibships of different sizes in each group, and since the variance of each cell is calculated separately, it is quite simple to apply appropriate weightings to the figures and derive more delicate significance tests than that given above.

**Results.**—Analysis of the figures by these methods shows that all four initial propositions are satisfied. In the subgroup with a negative family history there is a gross and significant excess of all-male sibships; the corresponding reduction in the mixed and female sibships affects them proportionately. The group with a positive family history shows a reasonably close correspondence between observed and expected numbers with regard to male, female, and mixed sibships.

Table VII sets out the crude figures with only children (solitaries) excluded. Table VIII shows that the inclusion of solitaries gives a similar result.

**Table VII**

<table>
<thead>
<tr>
<th>Group</th>
<th>Expected</th>
<th>Observed</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History Positive all-female</td>
<td>8.8</td>
<td>7</td>
<td>-1.8</td>
</tr>
<tr>
<td>all-male</td>
<td>10.0</td>
<td>4</td>
<td>-6</td>
</tr>
<tr>
<td>Family History Negative all-female</td>
<td>12.7</td>
<td>9</td>
<td>-3.7</td>
</tr>
<tr>
<td>all-male</td>
<td>14.5</td>
<td>30</td>
<td>+15.5</td>
</tr>
</tbody>
</table>

**Table VIII**

<table>
<thead>
<tr>
<th>Group</th>
<th>Expected</th>
<th>Observed</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibships all-male</td>
<td>36.5</td>
<td>57</td>
<td>+20.5</td>
</tr>
<tr>
<td>all-male</td>
<td>33</td>
<td>24</td>
<td>-9</td>
</tr>
<tr>
<td>Sibships mixed</td>
<td>52.5</td>
<td>41</td>
<td>-11.5</td>
</tr>
</tbody>
</table>

(a) For the all-male sibships: \( \frac{(\Sigma N_m - \Sigma E_m)}{\sqrt{\Sigma \text{Var}}} = 4.5 \).

(6) Three bastard propositions omitted from this table.

A finding of this kind requires confirmation and a second series of 137 consecutive cases was therefore analysed in a similar fashion. The results again satisfied our initial propositions.

The two samples, when combined, provided 337 sibships containing 827 children. The gross distribution of single-sex sibships for the combined sample is set out in Table IX. It will be seen that in the group with a positive family history families consisting entirely of girls are as common as those consisting entirely of boys (28:26), whereas, in the negative group the all-male sibships are in gross and significant excess (39:89).

**Table IX**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Sibships Containing Boys Only</th>
<th>Number of Sibships Containing Girls Only</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history positive..</td>
<td>26</td>
<td>28</td>
<td>54</td>
</tr>
<tr>
<td>Family history negative..</td>
<td>89</td>
<td>39</td>
<td>128</td>
</tr>
<tr>
<td>Totals .. ..</td>
<td>115</td>
<td>67</td>
<td>182</td>
</tr>
</tbody>
</table>

\( \chi^2 = 7.463. \ P \text{ is less than } 0.01. \)

(i) The 333 sibships contained in all 823 children.

(ii) There were four bastards, who have been excluded.

It seems then that a significant excess of all-male sibships is present in this example and is limited strictly to the subgroup in which no family history of fits was obtained.

We may now question whether we are dealing with a tendency to bear *more* boys than girls or whether the tendency is to bear all boys and no girls. This we may test by examining the sex ratio in the mixed sibships of the negative group and comparing this ratio with that in the single-sex sibships in the same group. Table X set out the figures for Series I. The results are quite clear.
cut. There is no excess of males in the mixed sibships; the sex ratio is, in fact, 95 males per 100 females. The whole excess of males is located in the single-sex sibships, and in this group the sex ratio is 306 males per 100 females.

TABLE X

THE SEX RATIO IN MIXED SIBSHIPS AND IN SINGLE-SEX SIBSHIPS COMPARED IN THE GROUP WITH NEGATIVE FAMILY HISTORIES (SERIES I)

<table>
<thead>
<tr>
<th>Group</th>
<th>Boys</th>
<th>Girls</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drawn from mixed sibships</td>
<td>71</td>
<td>75</td>
<td>146</td>
</tr>
<tr>
<td>Drawn from single-sex sibships</td>
<td>104</td>
<td>34</td>
<td>138</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>175</strong></td>
<td><strong>109</strong></td>
<td><strong>284</strong></td>
</tr>
</tbody>
</table>

Sex ratio in mixed sibships: 95 males per 100 females.
Sex ratio in single-sex sibships: 306 males per 100 females.

We set out by showing that there were more boys than girls with fits. We are now led to conclude that this is due solely to the existence of an excess of all-male sibships, limited to the subgroup with a negative family history of seizures.

Discussion

Sex Ratio.—One of the most curious problems of medicine is the tendency of diseases to attack one sex more than another. A differential sex ratio is usually placed under the heading of "aetiology", with the implication that some factor peculiar to the predominating sex is a contributing cause of the disease under study.

Examples of such selective incidence are rheumatoid arthritis (Trousseau, 1871), ankylosing spondylitis (Stone, 1947), acute intestinal obstruction (McIver, 1933), pyloric stenosis (Sheldon, 1943), coronary disease (White, 1945), rheumatic chorea (Lewis-Jonsson, 1949), mental defect (Sjögren, 1932 and 1935; Rosanoff, 1931). This list might be extended indefinitely.

The usual method of expressing a selective incidence is to divide a series of cases into males and females and to work out what percentage of the whole series was male and what percentage female. Clearly this must be the first step, but to use a ratio found in this way as an expression of the aetiological force of sex is open to grave objections. As we have shown the convulsive disorders of children are a case in point. Here the simple division of propositi into males and females has suggested to several workers that there is in male children an inherently greater tendency to fits.

Our findings suggest that this deduction is invalid.

Alström (1950) examined the sex ratio among adult Swedish epileptics as part of a thorough analysis of the genetics of the disease. He divided his series into those of "known", "probable", and "unknown" aetiology, the term "known" being roughly equivalent to "acquired", "organic", "post-traumatic", and the term "unknown" being equivalent to "idiopathic", "essential", or "genetic" epilepsy in other terminologies.

He showed that in the group of unknown aetiology (idiopathic epilepsy) the sex ratio was almost exactly 1:1; in the groups where the aetiology was thought to be definitely or probably known (acquired epilepsy) there was an excess of males of the order 177 males per 100 females. Alström deduced that the overall excess of males in his sample (55%) was due to the greater liability of males to acquire epilepsy through cerebral trauma of various types. The figures presented in previous sections of this paper suggest that deductions of this type should be re-examined.

There is, in fact, a close correspondence between Alström's figures and the findings of the present study. Thus the ratio in Alström's group of "cause unknown" (idiopathic epilepsy) is the same as that found in our children with a positive family history of fits. In Alström's series the ratio was 102 and in mine 105 males per 100 females. Among patients in whom the cause was "known" or "probable" in Alström's series the ratio was 177% compared with a ratio of 160% among those with negative family histories in the present sample (Table XI).

TABLE XI

THE SEX RATIO IN SWEDISH EPILEPTICS COMPARED WITH THOSE OF THE PRESENT SERIES

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Males per 100 Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alström (aetiology unknown) 606 cases</td>
<td>102</td>
</tr>
<tr>
<td>Ounsted (family history positive) 75 families</td>
<td>105</td>
</tr>
<tr>
<td>Alström (aetiology known or probable) 291 cases</td>
<td>177</td>
</tr>
<tr>
<td>Ounsted (family history negative) 125 families</td>
<td>160-2</td>
</tr>
</tbody>
</table>

But as we showed, when whole sibships are considered it is found that there is also an excess of males, of similar order, among the unaffected children, both in the sample as a whole, and in the subgroup with the negative family history. We were, therefore, forced to conclude that sex
was not a significant determinant, in spite of gross favouring of males among the propositi.

In some diseases the explanation for partial or complete sex-limitation is clearly genetic. Haemophilia is the classic example and provides the simple model. A single recessive gene with a locus on the X-chromosome is such that there is no allelomorph upon the Y-chromosome and necessarily limits the disease to males. Certain other recessively determined diseases of children show a sex ratio favouring males. Penrose (1949) cites albinism, familial diplegia and paraplegia, retinitis pigmentosa, amaurotic idiocy and low-grade defectives generally. He considers the theory of Sjögren (1932 and 1935) and Rosanoff (1931) that sex-linked genes are modifying factors, but he concludes that

"There seem to be no objections to the simple view that the genes concerned are differently manifested because the sexes are constitutionally different. It appears likely also that the variations in reaction within the sexes to different abnormal genes depend chiefly upon autosomal constitution."

Sex ratios should then be used with great caution even when the disease is genetically determined.

Diseases due to infection may also appear to show a selective sex incidence. Breen and Benjamin (1950) in a study of the 1947 and 1949 poliomyelitis epidemics in London found that in the age-range 1–4 years the sex ratio was 137 males per 100 females, but that the excess of males disappeared with rising age, and after puberty was replaced by an excess of females. In fact, then, the change in the sex ratio with age for poliomyelitis follows the same shaped curve as the change in the sex ratio in the general population (Royal Commission on Population, 1949). At the lower end of the scale the excess of males is likely to be due in part to an overall excess of males in the exposed population.

Our findings suggest that whether genetic factors or exogenous factors appear paramount in the aetiology of a disease an examination of the ratio in unaffected siblings should be made before any aetiological weight is given to the sex ratio in those affected.

The Inherited Factor.—In a pilot analysis of the family-trees of the patients in these samples (Ounsted, 1952) it was suggested that our methods of examining the role of heredity in convulsive disorders were necessarily inexact. In the present analysis we made therefore the most simple division of patients possible, allocating them into two groups, those with a positive and those with a negative family history. In practice this division seems justified by the results obtained, for it clearly isolates the subgroup containing the whole excess of males.

It is of interest that the pattern of sex ratio was the same for children with epilepsy as for those with convulsions. This finding is in agreement with the suggestion (Ounsted, 1952) that epilepsy and convulsions do not segregate from one another.

Single-Sex Sibships.—It is not difficult to construct a genetic model that would generate sibships consisting wholly of girls. A single recessive sex-linked gene lethal to the male foetus would suffice. All-male sibships present more difficulty, and since the genetics of the convulsive disorders are in any case nebulous, a model cannot justifiably be designed to explain our figures at this stage. It may well be that the all-male sibships were attracted into this sample by some purely environmental cause. Head injury is the natural suspect and a more detailed enquiry into this possibility is in progress. The finding that the excess of males affects equally those families derived from children with febrile convulsions and those with epilepsy, suggests, however, that a diathetic rather than an environmental factor is responsible.

That the preponderance of boys in this sample is due wholly to the existence of an excess of all-male sibships in the subgroup with a negative family history seems clear on simple inspection of the figures. The crude significance tests given appear to be reliable, for the application of more refined methods involving weighting techniques made only minor changes in the derived probabilities.

Finally it is interesting that the tendency of these families to generate males seems to be an all-or-none property. Mixed sibships make no contribution to the excess of males. The whole excess of males in the sample is located in single-sex sibships within the subgroup with the negative family histories.

Summary

In common with other authors we find more boys than girls affected with convulsive disorders of all types. Samples containing 337 personal consecutive cases with their 490 siblings were analysed.

Examination of the brothers and sisters of such patients shows, however, that there is also an excess of unaffected boys within the sibships.

Comparison with the sex ratio in the general population suggests that there is a tendency for sibships collected in this way to contain a true overall excess of surviving males.

Within the sample, however, the sex of a child does not affect its chance of developing a convulsive syndrome.
CHRISTOPHER OUNSTED

The excess of boys, both affected and unaffected, is limited strictly to a subgroup defined by a negative family history of seizures.

The excess is further limited to single-sex sibships and the existence of these all-male sibships accounts for the sex ratios discovered.

The findings suggest that the use of a differential sex ratio to measure the aetiological weight of sex is a suspect procedure.

No genetic model can justifiably be constructed to explain our findings at this stage.

I wish to thank Dr. V. Smallpeice, who supervised this work, for continuous encouragement and help; Mr. E. J. Finney and Dr. Sampford for much helpful assistance on the statistical analyses; the Research Advisory Sub-Committee of the Oxford Regional Hospital Board for valuable support.

REFERENCES

Scholarships in Aid of Scientific Research

The Council of the British Medical Association is prepared to receive applications for research scholarships, as follows:

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Applications for scholarships must be made not later than March 1, 1954, on the prescribed form, a copy of which will be supplied by me on application.

Applicants are required to furnish the names of three referees who are competent to speak as to their capacity for the research contemplated.

A. MACRAE,
Secretary.

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THE SEX RATIO IN CONVULSIVE DISORDERS
WITH A NOTE ON SINGLE-SEX SIBSHIPS

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J Neurol Neurosurg Psychiatry 1953 16: 267-274
doi: 10.1136/jnnp.16.4.267

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