Gynaecomastia and premature thelarche in a schoolchildren population of northern Italy

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Abstract
The prevalence and incidence of gynaecomastia and thelarche have been studied in pre-school children and school children belonging to different socio-economic classes in two Northern Italian Cities: Milano and Mantova. The children selected underwent three clinical examinations in their own school by the same examiner. The highest prevalence (36.6%) of breast enlargement was observed in nursery children until 2 years of age in Milano. Age and sex specific incidence rates were higher in Milano than in Mantova except in boys 11-14 years old. Assumption of drugs which might induce gynaecomastia thelarche was excluded. Relative risks calculated for veal and chicken must suggest that these are not relevant in the ethiology of breast enlargement.

Introduction
The incidence of gynaecomastia and premature thelarche in children has been increasing in different countries in the last few years. The physician is often faced with a problem which hardly fits into a clear diagnostic frame. The addition of oestrogenic and auxinic substances to cattle feed has already been implicated (Editorial 1982). Some of the recent epidemics of gynaecomastia and premature thelarche in groups of children eating in school cafeterias could be due to ingestion of such substances in the meat. After an epidemic of gynaecomastia and premature thelarche in a Milano school, the boys in five schools of the same city were studied between 1977 and 1978 as a comparison group (Fara et al 1979). The prevalence of gynaecomastia in the young (11 through 14 y.) subjects was about the same (34.6%) as in an epidemiologic study in the United States in the Sixties, and the prevalence of premature thelarche varied between 21.6% and 67.1% in girls (3 through 7 y.) (Nydict et al 1961). We have recently performed a clinical investigation on the diffusion of this phenomenon, not only in schoolchildren but also in children aged 2 to 5 y., because - to our knowledge - there are non epidemiologic investigation in the literature on the frequency of gynaecomastia.

Sampling and study methods
The subjects of this cross-sectional study were attending nurseries, kindergartens and schools of two northern italian cities (Milano and Mantova). These cities show different socio-economic features: Mantova is mostly rural and Milano is the largest italian trade center. About 1700 children were classified according to the following criteria: children aged 6 m. to 3 y. from nurseries, children in preschool and primary school (boys aged 3-10 y. and girls aged 3-7 y.), boys in secondary school (aged 11-14 y.). Only some of these schools have cafeterias. The schools were selected to guarantee random socio-economic levels of the children. Pupils of both well-off and working-class families were thus involved. Preliminary clinical examinations were performed during the an -
nual routine medical surveillance of the school population required by the re-
genral school health program.

Children were then submitted to two further examinations, every three months, by the same physician. In the physical examination the presence of glandular mammary tissue and the size of subareolar masses were assessed separately for each breast. Local pain and increased areolar pigmentation were recorded. Tanner's classification of breast size and Nydick's classification (Nydick 1961) of gynaecomastia were used: enlargement limited to the subareolar area and not reaching the margins of the areola is rated as (+), enlargement extending just to the areola margins is described as (++) and enlargement extending beyond the areola is described as (+++). Obese children (more than 20%) of ideal weight and more than 85% percentile of skinfold thickness) and girls of more than 7 years of age were excluded. None of the children considered presented symptoms of endocrine disease. The pupils' parents were directly asked on their child-
ren's habits regarding their diet and the medicines taken (if any) that might have induced breast enlargement. The information was to cover a period of three weeks before the subjects entered the study. The data collected were analyzed with regard to prevalence of breast enlargement detected at the first examina-
tion and incidence density of new cases detected during further visits. Popula-
tion considered at risk of developing breast enlargement consisted of children without gynaecomastia or premature thelarche at first observation. Relative risk estimating the effect of exposure to suspected oestrogenic factor, in-
gested through food, on breast enlargement, were also assessed.

Results

Over 93% (1140 subjects out of 1217) and over 98% (523 subjects out of 531) of the selected children completed physical examinations in Milano (MI) and Mantova (MN). Drop out rates of the two groups ranged from 0 to 11%, de-
pending on age and sex. The highest percentages of withdrawals both in Milano and Mantova were among children aged 3 to 5 years, who did not attend compul-
sory schools.

Moreover, 3.3% of the pupils' parents in Milano and 2.3% in Mantova re-
fused to be interviewed. Tab. 1 shows the distribution of breast enlargement prevalence and the 95% confidence intervals, with regard to age and sex. The frequency of cases was always greater in Milano than in Mantova.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Nº examined</th>
<th>Nº cases (prevalence %)</th>
<th>Confidence Interval (p=0.95)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MI</td>
<td>MN</td>
<td>MI</td>
</tr>
<tr>
<td>1-2</td>
<td>M</td>
<td>133</td>
<td>-</td>
<td>28</td>
</tr>
<tr>
<td>1-2</td>
<td>F</td>
<td>123</td>
<td>-</td>
<td>45</td>
</tr>
<tr>
<td>3-5</td>
<td>M</td>
<td>210</td>
<td>86</td>
<td>4</td>
</tr>
<tr>
<td>3-5</td>
<td>F</td>
<td>185</td>
<td>84</td>
<td>10</td>
</tr>
<tr>
<td>6-10</td>
<td>M</td>
<td>305</td>
<td>189</td>
<td>17</td>
</tr>
<tr>
<td>6-7</td>
<td>F</td>
<td>143</td>
<td>113</td>
<td>13</td>
</tr>
<tr>
<td>11-14</td>
<td>M</td>
<td>118</td>
<td>59</td>
<td>37</td>
</tr>
</tbody>
</table>

Tab. 1: Prevalence of gynaecomastia and thelarche by age and sex groups.
It is striking that gynaecomastia an premature thelarche are particularly and surprisingly frequent in Milano nursery children (21.1% for boys under 2 years and 36.6% for girls). Firm subareolar masses and thelarche were observed in about 19% of girls, with nodules reaching the margin of the areola (with a diameter of more than 0.5 cm). In more than 2% of these cases, the mass was even larger. The higher prevalence of manifestations in boys aged 11 to 14 y. (Milano: 31.4%, Mantova: 25.4%) is consistent with data in the literature (Fara et al 1979). The incidence densities are listed in tab. 2.

<table>
<thead>
<tr>
<th>Person/trimester</th>
<th>Age</th>
<th>Sex</th>
<th>Sex at risk</th>
<th>N° cases (incidence %)</th>
<th>Conf. Inter. (p=0.95)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MI</td>
<td>MN</td>
<td>MI</td>
</tr>
<tr>
<td>1-2</td>
<td>M</td>
<td>175</td>
<td>-</td>
<td>33(18.8)</td>
<td>13.3-25.4</td>
</tr>
<tr>
<td>1-2</td>
<td>F</td>
<td>115</td>
<td>-</td>
<td>33(28.6)</td>
<td>20.6-37.9</td>
</tr>
<tr>
<td>3-5</td>
<td>M</td>
<td>390</td>
<td>171</td>
<td>13(3.3)</td>
<td>1.8-5.6</td>
</tr>
<tr>
<td>3-5</td>
<td>F</td>
<td>331</td>
<td>164</td>
<td>14(4.3)</td>
<td>2.3-7.0</td>
</tr>
<tr>
<td>6-10</td>
<td>M</td>
<td>549</td>
<td>369</td>
<td>27(4.9)</td>
<td>3.3-7.1</td>
</tr>
<tr>
<td>6-7</td>
<td>F</td>
<td>246</td>
<td>207</td>
<td>14(5.7)</td>
<td>3.1-9.4</td>
</tr>
<tr>
<td>11-14</td>
<td>M</td>
<td>143</td>
<td>71</td>
<td>22(15.3)</td>
<td>9.9-22.4</td>
</tr>
</tbody>
</table>

* calculated by the Poisson distribution

Tab. 2: Incidence of gynaecomastia and thelarche by age and sex groups.

Incidence values agree with the data of prevalence. Indeed, age and sex specific incidence rates were higher in Milano than in Mantova, except for boys 11-14 y. On the other hand, the incidences of gynaecomastia (18.8%) and premature thelarche (28.6%), as recorded in Milano nursery children 1-2y. of age, are higher than the rates of breast enlargement in other groups.

The risk factors suspected to be associated with breast enlargement were analyzed to assess the importance of veal or chicken meat (when eaten at least once a week). The relative risk for breast enlargement for veal and chicken meat consumers vs. non-consumers is greater than one (2.3) only for girls of Mantova aged 6 to 7 years, though not statistically significant. Relative risks calculated for chicken meat (all are lower than one) suggest that this factor is not relevant in the ethiology of breast enlargement.

Discussion

Premature thelarche (before 8 y. of age) and gynaecomastia have been of growing importance in the last few decades with varying clinical features (Mills et al 1981, Perez Comas 1982, Bongiovanni 1983, Fara et al 1983).

Sometimes there is only a moderate quantity of sub-areolar glandular tissue, rapidly and easily distinguishable from the surrounding adipose tissue. Alternatively, there are glandular swellings, sometimes diffuse, which are hard to distinguish from the surrounding adipose tissue. The risk factors of gynaecomastia and premature thelarche may be quite different. It is well known that gynaecomastia and premature thelarche are normal phenomena in the neona-
tal period and the first weeks of life. Furthermore, gynaecomastia is often found in prepuberal subjects and for this age class there are some interesting data in the literature about american teen-agers (Nydick 1961). The most significant epidemiologic works are those of Nydick et al (1961) and Harlam and Grillo (1978).

The prevalence of the disease in their studies are very different (38.7% and 8.2%). These data indicate that in the last decades there could have been en
vironmental and alimentary changes in the USA which explain the marked reduction in the clinical manifestations in the latter study. There are other reports in the literature that show that many cases of gynaecomastia or premature thelarche occur after prolonged treatment with some drugs as: busulfan, digitalis, spiro-

During the last decade about 600 cases of premature thelarche and preco
cious sexual development have been reported in Puerto Rico by different studies (Bongiovanni 1983, Perez Comas 1982). These data are particularly striking for an island population of only 3 millions. The hormonal tests performed so far did not reveal endocrinologic abnormalities. Therefore, the different investiga
gators suggest that these clinical manifestations are the result of exposure to exogenous oestrogens or to oestrogen-like substances. The analysis of the pre
nenent data reveals some important characteristics of breast enlargement for the different group examined and the different ages of the subjects at the time of its appearance. Prevalence and incidence by age and sex of gynaecomstia and pre
mature thelarche are definitely greater in Milano than in Mantova. Comparison between rates of Milano and Mantova were performed. The differences observed are attributable to chance fluctuations in the two groups, except for incidence in male 3-5 y. (p=0.009) and 6-10 y. (p=1.3 x 10^{-5}). Conclusive explanations of this result should be drawn with caution because of extremely small number of cases occurred in these classes of age. As observed in Milano (31.4%) gy
naecomastia is frequently detected in the puberal population (boys 11-14 y of age); this may be a normal phenomenon in male. There is also growing evidence that breast enlargement is very common in Milano in early childhood as well. At present, we cannot give a satisfying explanation for this finding. One factor that should be studied is the role of difference in nutrition during infancy in the induction of breast enlargement. The results of the present study do not reveal any single risk factor as strictly related to breast en
largement, although some environmental toxin, perhaps an animal growth addi
tion, might account for any geographic difference.

Study of dietary habits, performed under controlled situations (i.e; boarding schools or orphanages), in order to avoid differences in diets other than at noon, should be undertaken. To investigate the importance of dietary differences, in the hope of detecting still unknown risk factors, an interna
tional multicentric study should be carried out.

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References
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