peripheral blood cell counts. With the method of preparing the nucleic acids used by these authors, degradation of the nucleic acids and heavy protein contamination was to be expected and the transfer of intact templates may probably be excluded. Non-specific stimulation of the hemopoiesis by thymidine residues and analogues was probably the mechanism of action in this case. This and similar works established the basis for the therapeutic use, now discontinued, of nucleotides in aplastic anaemia to stimulate hemopoiesis. However, the problem is to stimulate hemopoiesis and another is to redifferentiate anaplastic leukaemic stem cells. Further evidence for true redifferentiation of the leukaemic cells may have to be gained by the use of normal RNA on cultures of leukaemic cells in the absence of potentially hemopoietic normal reticulum cells.


21 Wilkins, M. H. F., and DeCarvalhalo, S., Blood, 8, 344 (1956).

**CHANGE OF HUMAN CHROMOSOME COUNT DISTRIBUTIONS WITH AGE: EVIDENCE FOR A SEX DIFFERENCE**

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AND

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| Age group No. of Mean (±) subjects ages y. | No. of cells with expressed as % of diploid cells
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>0-4</td>
<td>10</td>
</tr>
<tr>
<td>5-14</td>
<td>13</td>
</tr>
<tr>
<td>15-24</td>
<td>22</td>
</tr>
<tr>
<td>25-34</td>
<td>21</td>
</tr>
<tr>
<td>35-44</td>
<td>8</td>
</tr>
<tr>
<td>50-54</td>
<td>6</td>
</tr>
<tr>
<td>55-64</td>
<td>10</td>
</tr>
<tr>
<td>65-74</td>
<td>10</td>
</tr>
<tr>
<td>75+</td>
<td>11</td>
</tr>
</tbody>
</table>

**All ages** | 124 | 30.15 | 421 | 210 | 316 | 16 | 12-92 | 4-49 |

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**Table 1. DISTRIBUTION OF CHROMOSOME COUNTS AT AGE AND CHROMOSOMAL SEX**

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was not possible, but a partial analysis could be made. Such cells in males were included with those fully analysed even though the chromosome count could only be ascribed to the M/L group, and in females where the chromosome count could only be ascribed to the S group (S₁-S₄).

In group L, autosomes Nos. 1, 2 and 3 can of course be recognized as individual entities, but so few cells contained an abnormal number of L autosomes that this refinement was omitted. In the subsequent analyses of the aneuploid cells, those cells have been omitted which were of too poor a quality for full analysis, together with all cells carrying structural chromosomal abnormalities. Furthermore, cells with a chromosome count of 43 or less have also been discarded as many or all are likely to be artefacts due to rupture of the cell. The distributions of the counts in the remaining cells are given in Table 2; the results show that the proportion of hypodiploid cells still increased with age, and that the regression coefficients still differed significantly (P < 0.01). In this and the subsequent analyses the numbers of hypodiploid cells were found to be too small for any valid conclusions to be drawn.

Table 2. DISTRIBUTION OF CHROMOSOME COUNTS BY SEX AND AGE AFTER EXCLUSION OF CERTAIN GROUPS OF ANEUPLOID CELLS

<table>
<thead>
<tr>
<th>Chromosomal sex</th>
<th>Age group (yr.)</th>
<th>No. of cells with chromosome counts &lt; 46</th>
<th>Cells with hypodiploid (hypodiploid) counts</th>
<th>Percentage of diploid cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>0-14</td>
<td>17</td>
<td>3</td>
<td>2.05</td>
</tr>
<tr>
<td></td>
<td>15-34</td>
<td>25</td>
<td>5</td>
<td>2.05</td>
</tr>
<tr>
<td></td>
<td>35-44</td>
<td>45</td>
<td>5</td>
<td>3.01</td>
</tr>
<tr>
<td></td>
<td>45-54</td>
<td>24</td>
<td>2</td>
<td>4.22</td>
</tr>
<tr>
<td></td>
<td>55-74</td>
<td>29</td>
<td>10</td>
<td>6.52</td>
</tr>
<tr>
<td></td>
<td>75-1</td>
<td>152</td>
<td>24</td>
<td>9.54</td>
</tr>
<tr>
<td></td>
<td>9-124</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0-14</td>
<td>26</td>
<td>4</td>
<td>2.18</td>
</tr>
<tr>
<td></td>
<td>15-34</td>
<td>29</td>
<td>2</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>35-44</td>
<td>44</td>
<td>10</td>
<td>2.30</td>
</tr>
<tr>
<td></td>
<td>45-54</td>
<td>21</td>
<td>5</td>
<td>4.90</td>
</tr>
<tr>
<td></td>
<td>55-74</td>
<td>29</td>
<td>5</td>
<td>6.67</td>
</tr>
<tr>
<td></td>
<td>75-1</td>
<td>33</td>
<td>5</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>All ages</td>
<td>137</td>
<td>33</td>
<td>3.65</td>
</tr>
</tbody>
</table>

Regression on age of the percentage of:

- SELECTED hypodiploid cells, sex M: $y = -0.095x + 2.39$
- SELECTED hypodiploid cells, sex F: $y = 0.004x - 0.40$

Both regression coefficients are significantly different from zero (P < 0.01)

* See text for definition. The number of subjects, their mean ages and the numbers of diploid cells counted in each group are given in Table 1.

Inspection of the data suggested that in males an undue proportion of the hypodiploid cells was missing an S₁ chromosome, whereas in females an undue proportion was lacking an M chromosome. The proportion of hypodiploid cells not only increases with age (Table 3), but also these cells account for nearly all the regression on age previously observed. If these cells are excluded then the regression of the remaining hypodiploid cells on age becomes extremely small, and the coefficients do not differ significantly from zero in either sex (males, $y = 0.006x + 2.15$; females, $y = -0.005x + 1.41$).

The results reported here are open to criticism on the grounds that the observations were not made on a representative sample of the general population. The subjects were comprised of healthy volunteers, hospital in-patients, parents of children with chromosomal abnormalities, etc. To offset this difficulty a study is in progress of a group of subjects selected at random from the lists of general practitioners. This investigation will eventually include men and women of all ages from 15 years and upwards, but so far data only referable to those of 65 years and more are available. These, however, confirm the findings already noted for this group, and in this study every cell has been fully analysed. Examination of 1,050 cells from 35 males (mean age 71-69 years) shows 9-26 per cent to be aneuploid and that the proportions increase progressively for the age-groups 65-69, 70-74 and 75-79 and 80 years and over, being respectively 7-14, 10-09 and 12-15 per cent. 48 cells with 45 chromosomes were available for analysis, 27 of which were missing an S₁ chromosome (expected number on the basis of random loss, 5-22). In 12 of these cells the missing chromosome could confidently be said to be a Y chromosome, whereas only 1-04 such cells would be expected if all chromosomes had an equal chance of being lost. The findings from the analysis of 1,290 cells from 45 females (mean age 73-49 years) again confirmed the earlier findings. The proportion of aneuploid cells was 11-50 per cent and this proportion did not change progressively for the age-groups 65-69, 70-74, 75-79 and 80 years and over, the relevant proportions being 11-37, 12-08, 11-94 and 10-20 per cent. 95 cells with a count of 45 chromosomes were available for analysis, of which 81 were missing an M chromosome (expected number on the basis of random loss, 33-04). The substantial agreement between the earlier and later findings for ages of 65 years and more does indicate that it is unlikely that any serious bias has been introduced into the earlier findings due to the composition of the study population.

It seems reasonable to postulate that the observed increases in the proportion of aneuploid cells with age, which in males is mainly due to the loss of an S₁ chromosome and in females to the loss of an X chromosome, is in fact largely due to divisional errors involving the Y chromosome in men and the X chromosome in women. Direct evidence is available for the Y chromosome as in good preparations it is identifiable, and therefore its absence is recognizable. Direct evidence for the involvement of the X chromosome is not yet available, but it may become so from techniques using tritiated thymidine labelling. It may well also be relevant that the major change involving an M chromosome in women occurs at the time of a sharp decline in sexual activity. Both in males and females the findings could be explained: (1) if there was a special liability for cells to lose a sex chromosome, or (2) if all chromosomes were liable to be involved, but that the cells with an abnormal number of autosomes were at a disadvantage and failed to survive, or (3) if both possibilities occurred together.

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