THE WHITE CELL COUNT AND EXPOSURE TO RADIATION HAZARDS

THE SIGNIFICANCE OF LEUCOCYTE "WARNING" AND "REJECTION" LEVELS IN THE YOUNGER AGE GROUPS

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From time to time the medical officers examining new entrants to the Atomic Energy Research Establishment (A.E.R.E.) receive the impression that there is an undue proportion of low blood counts in the "apprentice age" personnel. This appears, in general, to take the form of a neutropenia, which may, in certain cases, throw doubt on the suitability of an applicant for work which might involve exposure to radiation. It seemed appropriate, therefore, to investigate the blood counts of all age groups to find out whether there was any statistical evidence to support this impression.

Method

Two sets of figures, based on estimates of the lower limits of normal, have been adopted at A.E.R.E. to act as a guide to doctors carrying out pre-employment medical examinations, one setting a "warning" level of blood count and the other a "rejection" level.

	Warning Level (mm. ³)	Rejection Level (mm. ³)
Leucocytes	4,500	3,000
Neutrophils	3,000	2,000
Lymphocytes	1,000	750

A candidate having a count at the former level would be accepted for employment, but would be exposed to radiation hazard only if and when it had been found that this was, in fact, his physiological level and that clinical signs of damage to or deficiency in the haemopoietic tissues were absent: a candidate with counts at or below the rejection level would be considered unsuitable for employment in an atomic energy establishment.

It has been shown by Chamberlain, Turner, and Williams (1952) that the first, or pre-employment count, is not the most reliable count on which to base a statistical investigation as it tends to be

inflated by emotional factors. However, in this instance, it was considered to be the appropriate figure to use, as it is from this evidence that the medical officer has to deduce whether an applicant is, or is not, suitable for appointment.

The data used consisted of the first counts of all potential new entrants examined during the two-year period July 1, 1952, to June 30, 1954; these numbered 1,897.

Results

The numbers and percentages of low counts for each type of cell in each age group are shown in Table 1.

TABLE 1
NUMBERS AND PERCENTAGES OF PRE-EMPLOYMENT
COUNTS BELOW "WARNING" AND "REJECTION"
LEVELS

Age Group	No. in Age Group	Leucocytes		Neutrophils		Lymphocytes	
		No. Below	% of Age Group Below	No. Below	% of Age Group Below	No. Below	% of Age Group Below
Below Warning Level							
16-19	340	12	3.5	83	24.4	2	0.6
20-29	735	19	2.6	119	16.2	6	0.8
30-39	403	3	0.7	47	11.7	1	0.3
40-49	248	7	2.8	27	10.9	1	0.4
50-59	128	3	2.3	18	14.1	0	0
60-69	43	2	4.6	6	14.0	0	0
Totals	1,897	46	2.4	300	15.8	10	0.5
Below Rejection Level							
16-19	340	0	0	9	2.6	0	0
20-29	735	0	0	10	1.4	2	0.3
30-39	403	0	0	2	0.5	1	0.3
40-49	248	0	0	4	1.6	0	0
50-59	128	0	0	2	1.6	0	0
60-69	43	0	0	3	7.0	0	0
Totals	1,897	0	0	30	1.6	3	0.2

These results show that low neutrophil counts would account for a greater number of rejections or "provisional" acceptances than would low lymphocyte counts: of the totals for all age groups 15.8% show warning level "neutropenia" as against 0.5%

"lymphopenia", and 1.6% show rejection level "neutropenia" compared with 0.2% "rejection" level "lymphopenia". Furthermore, the age group showing the highest number of counts below warning level, is, as was suspected by the medical officers, the 16-19-year-olds. Although the rejection rate in all groups is small, Table 1 shows that, over the range 16-60 years, the apprentice age group has a higher rejection rate than the older age groups: the 60-70-year-olds (a relatively small group) have the highest rejection rate (7%). There are no rejections based solely on leucocyte counts, and only 0.2% of all ages based on lymphocyte counts.

Whitby and Britton (1946) and various other workers, including Garrey and Bryan (1935) and Kolmer and Boerner (1945), state that the mean leucocyte count shows a tendency to fall with age over the years covering infancy to about 12 to 15 years, after which it tends to remain stationary, the effect of increased age being negligible (Gabbert, Hutaff, and Harrell, 1947). If this is the case it would be expected that in a normal working population the proportion of individuals with counts below rejection and warning levels would be the same for all age groups. Thus if the expected numbers below warning and rejection levels respectively for each age group are estimated on the assumption that the proportion of individuals with low counts would be the same for all age groups and those expected numbers are compared with the observed numbers, a χ^2 test can be made, results of which would not be expected to be significant. Total leucocyte counts showed good agreement between observed and expected numbers below warning level ($P = 0.25$): there were no leucocyte counts below rejection level. In the case of neutrophils, however, at warning level χ^2 is highly significant ($P < 0.001$), which is due in large measure to the excess of observed over expected figures in the youngest age group. Agreement is reasonably good at neutrophil rejection levels ($P \sim 0.1$), although here again there is an excess of observed over expected figures in the youngest age group. The numbers of lymphocyte counts below warning and rejection levels were too small to apply the χ^2 test.

The tendency towards low neutrophil counts in the youngest group is reflected in the level of the mean counts of that group when compared with those for the older groups (Table 2). The levels of lymphocyte counts are approximately the same for all groups.

It was considered possible (although unlikely) that the high proportion of "neutropenics" in the youngest age group might be due to absence of emotional effects in younger personnel; accordingly

TABLE 2
MEAN COUNTS OF NEW ENTRANTS ACCORDING TO AGE GROUPS (per mm.³)

Age Group	No.	Leucocytes		Neutrophils		Lymphocytes	
		Mean	S.E.	Mean	S.E.	Mean	S.E.
16-19	340	7,728	125	4,277	103	2,631	44
20-29	735	7,950	85	4,659	69	2,495	30
30-39	403	8,670	141	5,301	119	2,597	43
40-49	248	8,510	162	5,028	117	2,659	54
50-59	128	8,125	238	4,590	165	2,662	82
60-69	43	8,819	438	5,122	338	2,840	159
Total	1,897	8,168	57	4,761	46	2,581	19

a further survey on similar lines and covering the same period of time was made based on the second counts of randomly selected personnel not exposed to radiation. Details are given in Tables 3A and B.

TABLE 3A
NUMBERS AND PERCENTAGES OF COUNTS BELOW WARNING AND REJECTION LEVELS AT SECOND BLOOD COUNT

Age Group	No.	Leucocytes*		Neutrophils				Lymphocytes*	
		Warning Level		Warning		Rejection		Warning	
		No. Below	% of Age Group Below	No. Below	%	No. Below	%	No. Below	%
16-19	109	3	2.75	27	24.77	5	4.59	0	0
20-29	196	6	3.06	55	28.06	5	2.55	1	0.51
30-39	260	10	3.85	68	26.15	6	2.31	1	0.38
40-49	81	0	0	16	19.75	3	3.70	0	0
50-59	120	7	5.83	24	20.00	3	2.50	2	1.67
60-69	80	1	1.25	15	18.75	1	1.25	0	0
Total	846	27	3.19	205	24.23	23	2.72	4	0.47

* There were no leucocyte or lymphocyte counts below rejection level.

TABLE 3B
MEAN OF SECOND BLOOD COUNTS BY AGE GROUPS

Age Group	No.	Leucocytes		Neutrophils		Lymphocytes	
		Mean	S.E.	Mean	S.E.	Mean	S.E.
16-19	109	7,512	180	3,892	133	2,804	79
20-29	196	7,589	146	4,054	98	2,704	59
30-39	260	7,921	149	4,327	125	2,801	55
40-49	81	8,300	322	4,553	225	2,838	101
50-59	120	7,965	235	4,596	175	2,604	80
60-69	80	8,132	291	4,425	199	2,813	109
Total	846	7,854		4,277		2,756	

On the basis of second counts, a much higher percentage (ranging from 18 to 28) of neutrophil counts of all age groups falls into the warning category (Table 3A); similarly, although the figures are of more reasonable proportions (from 2% to 4%), an increase in the number of neutrophil counts at rejection levels is observed. Furthermore, the numbers of counts falling below warning or rejection levels now tend to be the same for all age groups. However, in the 16-19 age group the percentage at warning level remains the same as in the earlier estimate. Applying the χ^2 test as before, good

agreement is found between expected and observed figures for each age group, the figures for χ^2 not being significant for all types of cell at both levels.

Reference to Table 3B shows that, as was demonstrated in earlier work at A.E.R.E. (Chamberlain *et al.*, 1952), the means of second counts are, at all age levels, lower than those of first counts. However, the relative differences between the mean counts of the age groups remain substantially the same, *i.e.*, the lowest age groups have the lowest counts.

A further line of investigation to account for the high incidence of low neutrophil counts was suggested by evidence (Chamberlain *et al.*, 1952) that a seasonal variation occurs in mean counts, the lowest levels being reached in the quarter from July 1 to September 30. It would be expected that a high proportion of the 16-19 age group would take up employment for the first time during this period which is coincident with the end of the school year. This being so it would follow that a higher proportion of blood counts would be performed on this group than on older groups at the time of year when the count is known to be at its lowest. In order to test this hypothesis an estimate was made of the distribution by age and season of 5,687 new entrants during the years 1949-54, and also of the 1,897 new entrants here under consideration. It was found that approximately 70% of the 16-19-year-olds take up employment in the later half of the year, whereas distribution of the older age groups is spread more evenly throughout the year.

There remained the further possibility that the time of day during which the counts were made might affect the level of count. It has been shown by Shaw (1927) and confirmed at A.E.R.E. (Chamberlain *et al.*, 1952) that the neutrophil count is lowest in the morning, rising to a maximum in the late afternoon. Thus, if a greater proportion of counts was made on younger entrants than on older entrants in the morning a bias towards low counts in the former group would be imparted. Accordingly the counts of all new entrants for the year 1954 were analysed by time of count and age group: the results, shown in Table 4, give little support to this hypothesis.

TABLE 4
DISTRIBUTION OF NEW ENTRANTS (1954) BY AGE GROUP
AND TIME OF COUNT

Time	8 a.m.-10 a.m.	8 a.m.-1 p.m.	1 p.m.-5 p.m.	No. in Age Group
Age Group	% of Age Group	% of Age Group	% of Age Group	
16-19	52.45	66.24	33.76	154
20-29	45.16	64.08	35.92	465
30-39	49.08	61.53	38.47	273
40-49	66.25	71.88	28.12	160
50-59	72.63	82.11	17.89	95
60-69	78.79	90.91	9.09	33
				1,180

It will be observed that morning counts occur with greater frequency in the older age groups than in the younger age groups, although of the three younger decades the apprentice age group shows a slightly higher percentage of early counts.

Discussion

There is no doubt, on the basis of the standards laid down at A.E.R.E., that there is a higher proportion of individuals in the apprentice age group than in older age groups with pre-employment white cell (primarily neutrophil) counts below warning and rejection levels. Whilst there is little difference between all age groups in the number of "warnings" and "rejections" based on lymphocyte counts, and slightly more when based on leucocyte counts, there is a considerable difference between the 16-19-year-olds (24%) and the higher age groups (11%-16%) when the pre-employment neutrophil count is considered. It is difficult to find a satisfactory explanation of this phenomenon, particularly as, as mentioned earlier, the consensus of opinion appears to be that adult levels of counts are reached between the ages of 12 and 15 years. There is no information in the literature to suggest that a tendency towards low neutrophil counts exists during this period (16-19 years) of growth. Abbott, Ahmann, and Overstreet (1939), working with college students, women, and children in rural schools, observed that vitamin A deficiency appears to produce a slight leucopenia, chiefly affecting the neutrophils, but no evidence is available regarding the nutritional status of the population here under review to suggest that this might account for the low neutrophil counts in the youngest group. Nor can they be accounted for by the time of day at which counts are made. In fact, if this were the predominating factor affecting level of counts, it would be expected from the results in Table 4 that the lowest counts would be found in the higher age groups.

There is a possibility that the physiological response to emotion associated with and raising the level of first blood counts may be less in the apprentice age group than in older groups. Some support is lent to this theory by the results of the investigations on second counts reported in Table 3. This shows that although the mean of all second counts is lower than the first, the effect is less marked in the youngest group. Furthermore, the percentage of individuals below warning level in the youngest group remains the same for both first and second counts, but is increased in the older age groups.

A possible explanation of the excess of low counts in the apprentice age group is likely to be found in

the fact that the majority of its members begin employment and have their first count during the period of the year in which blood count levels are normally at their lowest. This means that any comparison made with other age groups, whose date of entry is spread out more evenly over the whole year, is likely to show a bias towards lower counts in this group. Furthermore, the depressing seasonal effect would be reflected in the mean of subsequent counts, when carried out on an annual basis.

It appears to the writer that, in the light of the results of this investigation, the use of a figure of 3,000 neutrophils per mm.³ as a warning level is unrealistic. Its use implies that, on the basis of a first count, 16%, or on the basis of a second count, 24%, of candidates would require careful medical supervision when considerations for exposure to radiation hazards arose. This, in what is assumed to be a cross-section of a normal healthy working population, seems to be an unduly high proportion; it would be expected that the findings for neutrophils would be of a similar order to those of leucocytes and lymphocytes and not five to eight times greater as is now the case. It is suggested therefore that a lower figure should be adopted. If a figure of 2,500 per mm.³ were used distribution of "warnings" between age groups would be as follows for first and second counts (Table 5).

TABLE 5
NUMBER AND PERCENTAGES OF NEUTROPHIL COUNTS
BELOW A WARNING LEVEL OF 2,500 CELLS PER mm.³

Age Group	First Count			Second Count		
	Neutrophils	No.	%	Neutrophils	No.	%
16-19	340	36	10.58	109	14	12.84
20-29	735	45	6.12	196	23	11.73
30-39	403	22	5.46	260	28	10.76
40-49	248	13	5.24	81	6	7.41
50-59	128	11	8.59	120	13	10.83
60-69	43	3	6.97	80	7	8.75
Total	1,897	130	6.85	846	91	10.75

The figures are still considerably higher than comparable figures for leucocytes and lymphocytes, particularly in the 16-19-year group, the warning rates being 7% and 10% for all groups and for the 16-19 age group respectively. A further reduction of 500 in warning level would bring the figures down to those of the present rejection level.

The adoption of a figure of 2,500 neutrophils per mm.³ would still be above the lower limits of the 95% range quoted by various authors:

	Neutrophils	95% Range
A.E.R.E. (1951) pre-employment	3,098	2,250-8,200
A.E.R.E. (1952-54)	1,897	2,100-9,500
Blackburn (1947)	642	856-7,352
Osgood <i>et al.</i> (1939)	269	1,500-7,500

Russ (1943) lists the lower limits of neutrophil counts regarded by 16 heads of hospital departments as incompatible with continuance of radiological work. Of these seven range from 2,000 to 2,500 and nine from 3,000 to 4,000 cells per mm.³ Robertson-Smith (1951) stated that the lower limit of normal for personnel working with radiation was changed in his establishment from 3,000 to 2,000 neutrophils per mm.³, as it was found that a considerable number of counts below 3,000 per mm.³ occurred in unexposed personnel.

The findings from this investigation suggest that, in order to avoid undue discrimination against the youngest age group as a result of low neutrophil counts, more latitude might be exercised regarding acceptable levels of count, so long as the clinical picture reveals no indication of haemopoietic deficiency. Haematological control could be maintained in this age group by taking blood counts at intervals sufficiently close to render it possible to acquire some information on the individual's basic norm.

Summary

An analysis has been made of the blood counts of 1,897 new entrants during the period July 1, 1952, to June 30, 1954, to determine the number with counts below "warning" and "rejection" levels in various age groups.

The number of individuals with neutrophil counts below these levels was found to be higher in the 16-19-year age group than in the older groups. There were also more warnings and rejections in all groups attributed to low neutrophil counts than to low leucocyte or lymphocyte counts.

An investigation into the distribution of age groups according to season of the year revealed that a higher proportion of apprentice age personnel began employment at the end of the school year, which coincides with the season at which blood counts are known to reach their lowest level.

The adoption of lower standards for warning and rejection levels of neutrophil counts is recommended.

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