

3rd December 1942

Professor R.A. Fisher, ScD., F.R.S.
South Eastern Experimental Agricultural Station,
ROTHAMSTED, Harpenden.

Dear Professor Fisher,

I shall feel greatly indebted to you if you can assist me in some difficulties I have encountered in calculating errors in blood counts.

The "absolute differential count" is now being used. It is performed in two stages. First, the total leucocyte count is determined using a haemocytometer. Second, a smear of blood is made between coverslips or on a slide, stained, and the leucocytes seen are classified into their different varieties: not less than 200 cells are classified, sometimes 2000, and the result for each type of leucocyte is expressed as a percentage. From the total count of leucocytes, and their percentage distribution in the stained film, the absolute number of each kind of leucocyte in a cubic millimetre of blood is calculated: thus, for example, in one case I found:

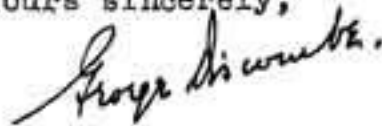
	<u>20.4.42</u>	<u>25.4.42</u>
Total leucocytes	4,600 per cu. mm.	5,400 per cu. mm.
Neutrophils:	49% or 2254 per cu. mm.	56% or 3024
Eosinophils:	2.5% or 115 " " "	3% or 162
Lymphocytes:	45% or 2070 " " "	40% or 2160
Monocytes:	3.5% or 161 " " "	1% or 54

I wish to be able to calculate the standard deviation of sampling of the absolute counts of neutrophils etc. I have no difficulty in calculating it separately for the haemocytometer count and for the differential count, but I do not understand how to combine them. For example, I do not think the variation in eosinophils or lymphocytes is likely to be significant, but I want a test which will tell me whether the change from 2254 to 3024 in neutrophils, or from 161 to 54 in monocytes is significant. It would be a convenience if the variance in this "absolute differential count" could be expressed as a function of the variances of the haemocytometer count and of the percentage count. This appears to me to be a special case of the problem of successive sampling, where from a universe samples either A or \bar{A} are drawn, and from the A sub-universe samples are drawn which may be $B\bar{Y}$, $\bar{B}C$, $\bar{B}\bar{Y}D$, etc. I have searched the literature as well as I can, but I cannot find any reference to the problem. Since I am not a trained statistician but apply the simpler methods to avoid drawing conclusions which are unwarranted, I venture to apply to you for help in tracing this problem, which I feel sure must have been attacked before.

I know that the solution of the errors of haemocytometer counts is usually attributed to "Student", Plum (Acta med. Scand. 1936), however, attributes it to Abbe-Sitzungsberichte der Jenaischen Gesellschaft für Medizin und Naturwissenschaft Jahrg, 1878, 12 Sitzung pp. XCVIII-CV. As the only British library which possesses this is the Bodleian, and because my routine duties are fairly heavy and prevent me from checking all my references at present, I have not consulted this journal. I mention it in case you are interested.

I hope I shall not trouble you too greatly by making this request; the answer would be great value to me in interpreting the many blood counts I have to do.

Yours sincerely,

A handwritten signature in cursive script, appearing to read "George Dickson".

Senior Demonstrator of Pathology.