Development, History, and Future of Automated Cell Counters

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KEYWORDS

• Automated cell counter • Hematology • Blood • Hemoglobin
• Electrical impedance counting • Flow cytometry • Point of Care • Light scattering

KEY POINTS

- The invention of the microscope allowed the differentiation and counting of blood cells.
- Automated blood cell counters have greatly improved the speed and accuracy of cellular blood analysis, using optical light scattering or changes in electrical current induced by blood cells flowing through an electrically charged small opening.
- Novel methods under development include the addition of new parameters to the complete blood count and white cell differential and the development of smaller, portable instrumentation and of devices that allow in-vivo analysis of blood cells.

"…for the blood is the life"
—Deuteronomy 12:23

INTRODUCTION

Even in antiquity, blood was recognized as a singular bodily fluid that was the essence of life, possessing mysterious properties that provided sustenance for human survival. The unraveling of those mysterious properties only became possible once blood could first be characterized according to the appearance and number of its particulate components. Those critical steps comprised, in the first instance, the development of microscopy, enabling the visualization of component blood cells, and subsequently advances made possible through the techniques to measure physical properties of the formed elements of the blood as well as the electronic means of capturing this information.

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Clin Lab Med 35 (2015) 1–10
http://dx.doi.org/10.1016/j.cll.2014.11.003 **labmed.theclinics.com**
0272-2712/15/$ – see front matter

Abbreviations

CBC	Complete blood count
FOV	Field of view
RBC	Red blood cell
SRS	Stimulated Raman scattering
WBC	White blood cell

The development of the optical microscope made it possible to visualize individual human and plant cells, as well as bacteria. Even the simplest microscope developed by van Leeuwenhoek more than 300 years ago allowed the observation that blood is composed of small red globules, and their size was eventually determined. Progressive developments in optical microscopy followed during the next 2 centuries, such as the addition of an eyepiece to form a compound microscope and improved optics, including objective lenses comprising several lenses to correct for distortions. The application of dyes by Paul Ehrlich in the late 1870s allowed, for the first time, differentiation between different white cell types.[1,2] By then, it was evident that the number of blood cells changes in many diseases and it therefore became clear that it was important to more accurately quantify cell number by doing a blood count. Laborious manual measurements were introduced in which measured volumes of blood were placed on a calibrated slide chamber and cells were counted one by one, the total number being calculated from the known volume and geometry of the chamber. Although still in practice today because of its simplicity, manual counting of cells is prone to large errors and is both time consuming and labor intensive. Automated methods for counting blood cells became a necessity, and engineers began to work together with hematologists to find solutions to this problem. Over the ensuing decades, flow-based cytometers using light, impedance measurements, or both, were developed. These devices provided a large number of parameters related to enumerating and identifying blood elements, including erythrocytes (red blood cells [RBCs]), leukocytes (white blood cells [WBCs]), and thrombocytes (platelets), and differentiating the various leukocyte subtypes. In addition, with the recognition that qualitative differences in the appearance of red cells relating to their size, shape, and degree of hemoglobinization connoted certain types of anemia, the ability to simultaneously and independently measure hemoglobin concentration and hematocrit (or packed cell volume), together with the red cell count, provided Maxwell Wintrobe[3–5] with the tools to promulgate a set of red cell indices that included the mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. This development allowed the morphologic classification of anemias into subtypes according to whether microcytic, normocytic, or macrocytic; and hypochromic, normochromic, or even hyperchromic according to degree of hemoglobinization. Later, it also became possible to quantify the size distribution of red cell populations, expressed as the red blood cell distribution width, thus enabling a further distinction into homogeneous and heterogeneous categories within each morphologic subtype.[6]

UTILITY OF A BLOOD COUNT

Of all the tissues in the body, the blood in circulation is the easiest and least invasive to sample. As such, a blood count represents a biopsy obtained through a simple venipuncture. A complete blood count (CBC) is therefore one of the most commonly used clinical laboratory tests. It provides a rapid and cost-effective assessment of various modalities of a patient's state of health as well as important clues to the