Applications and Diagnostic Potential of Dried Blood Spots

Dried blood spot (DBS) is the process of collection of blood spots, beginning with a finger or heel prick and spotting whole blood directly onto a filter paper. The filter paper is then left to dry at room temperature. Once dried, DBS can be stored with desiccant and shipped to laboratories for testing.[1] Ivar Christian Bang is credited for the development of the idea of using blood collected on a paper card made of cellulose. In 1913, Bang determined glucose from eluates of DBS.[2] In 1963, Guthrie published his famous method for the diagnosis of phenylketonuria from DBS obtained by a heel prick from newborns.[3]

Major advantages of using DBS, as documented in literature are as follows: (a) Volume of blood required is less compared to conventional venipuncture; (b) The potential risk of bacterial contamination and/or hemolysis with traditional method is minimal with DBS; (c) Collection collection of blood is easy, noninvasive, and economical; (d) Blood spots can be conserved for long periods with almost no deterioration of the analytes.[2]

All the procedures for using DBS, namely, collection of blood sample on filter paper, its further processing, and its storage and/or transport to the laboratory, have been fairly standardized and can be easily adopted by any center.[2,4] Specimens for DBS are collected by withdrawing blood from finger, heel, or toe through lancet-prick and applying few drops on to absorbent paper. The blood is allowed to fully saturate the filter paper and paper is then air-dried for several hours. These specimens are then stored in low gas permeability plastic bags, with added desiccant to reduce humidity.[5] In the laboratory, small disc of saturated paper is separated using automated or manual hole punch. This separated disc is further processed in a flat-bottomed microtiter plate. The blood is eluted out in phosphate-buffered saline containing 0.05% Tween 80 and 0.005% sodium azide overnight at 4°C. The resultant plate containing the eluates forms the "master" from which dilutions can be made for subsequent testing.[6] Recent automation solutions extract the sample by flushing an eluent through the filter without punching it out.[7]

Conventionally, DBS is being used for screening of neonates for congenital and inherited metabolic disorders.[8] Early uses of DBS include serological testing to diagnose syphilis, the detection of antibodies against measles, mumps, poliovirus, parainfluenza virus and respiratory syncytial virus, the identification of Shigella in feces dried onto filter paper, and the detection of antibodies to Schistosoma in DBS.[9]

Other important applications include DNA/RNA molecular methods; immunologic studies; and nutritional evaluations of infants, children, and adults.[8] With advancement in immunoassays and in molecular techniques, DBS is now being used for detecting hepatitis B virus surface antigen, antibodies to HBV core antigen, antibodies to the hepatitis C virus (anti-HCV), HCV RNA, and human immunodeficiency virus (HIV) 1-p24-antigen/anti-HIV 1/2 using either a fully automated platform or sensitive qualitative nucleic acid tests.[10] Other potential and emerging applications of DBS are toxicokinetic and pharmacokinetic studies, metabolic profiling, therapeutic drug monitoring, forensic toxicology, or environmental contamination control.[11] DBS protocols for several drug analytes such as acetaminophen, aspirin, bosentan, caffeine, diazepam, omeprazole, procaine, valsartan, and metformin have already been developed, thus making therapeutic drug monitoring an easier exercise.[12] Besides, DBS is being used for detection of many metabolic intermediates such as bile acids, carnitine, creatinine, hemoglobin variants, and homocysteine.[13]

With the advent of mass spectrometry, DBS-based mass spectrometric applications have become very popular for many newborn screening laboratories worldwide, and it is expected that arena of diagnosis will be revolutionized with this new application.

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References

1. Smit PW, Sollis KA, Fiscus S, Ford N, Vitoria M, Essajee S, *et al.* Systematic review of the use of dried blood spots for monitoring HIV viral load and for early infant diagnosis. PLoS One 2014;9:e86461.
2. Grüner N, Stambouli O, Ross RS. Dried blood spots – Preparing and processing for use in immunoassays and in molecular techniques. J Vis Exp 2015;97:e52619. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4397000/pdf/jove-97-52619.pdf. [Last cited on 2018 Feb 8].
3. Guthrie R. Blood screening for phenylketonuria. JAMA 1961;178:863. Available from: http://www.jama.jamanetwork.com/article.aspx?articleid=332184. [Last accessed on 2017 Dec 26].
4. Lakshmy R. Analysis of the use of dried blood spot measurements in disease screening. J Diabetes Sci Technol 2008;2:242-3.
5. Knudsen RC, Slazyk WE, Richmond JY, Hannon WH. Guidelines for the Shipment of Dried Blood Spot Specimens. Centers for Disease Control and Prevention: Office of Health and Safety: Biosafety Branch; 1995. Available from: http://www.fiocruz.br/biosseguranca/Bis/manuais/sangue/Guidelines%20for%20the%20Shipment%20of%20Dried%20Blood%20Spot%20 Specimens.pdf. [Last accessed on 2017 Dec 27].
6. Parker SP, Cubitt WD. The use of the dried blood spot sample in

epidemiological studies. J Clin Pathol 1999;52:633-9.
7. Ganz N, Singrasa M, Nicolas L, Gutierrez M, Dingemanse J, Döbelin W, *et al.* Development and validation of a fully automated online human dried blood spot analysis of bosentan and its metabolites using the Sample Card and Prep DBS System. J Chromatogr B Analyt Technol Biomed Life Sci 2012;885-886:50-60.
8. De Jesús VR, Mei JV, Bell CJ, Hannon WH. Improving and assuring newborn screening laboratory quality worldwide: 30-year experience at the Centers for Disease Control and Prevention. Semin Perinatol 2010;34:125-33.
9. Smit PW, Elliott I, Peeling RW, Mabey D, Newton PN. An overview of the clinical use of filter paper in the diagnosis of tropical diseases. Am J Trop Med Hyg 2014;90:195-210.
10. Ross RS, Stambouli O, Grüner N, Marcus U, Cai W, Zhang W, *et al.* Detection of infections with hepatitis B virus, hepatitis C virus, and human immunodeficiency virus by analyses of dried blood spots – Performance characteristics of the ARCHITECT system and two commercial assays for nucleic acid amplification. Virol J 2013;10:72.
11. Demirev PA. Dried blood spots: Analysis and applications. Anal Chem 2013;85:779-89.
12. Suva MA. A brief review on dried blood spots applications in drug development. J Pharm Biosci 2014;1:17-23.
13. Zakaria R, Allen KJ, Koplin JJ, Roche P, Greaves RF. Advantages and challenges of dried blood spot analysis by mass spectrometry across the total testing process. EJIFCC 2016;27:288-317.

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