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PEN SIDE DIAGNOSIS OF INFECTIOUS DISEASE- A CURRENT STATUS

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ABSTRACT

The development and evaluation of various test/ technologies for rapid and effective way of diagnosis of diseases is constantly felt in biomedical research. The traditional means of disease diagnosis is now a day's overcome by new exciting technological means because of its improve diagnostic capabilities besides reducing the time and cost, associated with conventional diagnostic techniques. Laboratory diagnosis for veterinary pathogens now has been improvised through the use of recombinant antigen, monoclonal antibodies and synthetic peptides, as well as incorporation of new molecular technique. Pen side diagnosis mostly has been felt for identification/detection of pathogens at field level in a rapid and accurate way particularly in disease outbreaks. Use of chromatographic strip, lateral flow technologies, immunoassay, biosensors, nanotechnology, mobile PCR assay are promising and hold great promise for improving speed and accuracy of diagnostics for various infectious pathogens in animals. The present paper reviews some of the current and potential use of pen side diagnostics in pathogens detections.

Key Words: Disease diagnosis, Livestock, Pathogen, Penside, Rapid

INTRODUCTION

In the recent diagnostics there is changing of paradigm to get faster rapid detection of diseases in the farmer's field level. Researcher has now developed several rapid diagnostic test/tools with varied sensitivity and specificity in diagnosis of important infectious diseases. The test could be performed before reaching to the laboratory and has termed to various synonyms as portable test, field test, on side test, pen side test, point of care test etc. The development of rapid and easy diagnostics has been felt long before and has reflected in various previous documents. For example the adsorption of influenza and mumps viruses into particles of lecithin-cholesterol provides antigens that are rapidly agglutinated by antisera in slide agglutination test (Klein et al 1966). Now a day in veterinary practise, the major consideration given to this group of test for cost benefit in terms of quicker results. For highly infectious diseases like FMD, HS, VS etc. decision of positivity or negativity is very much required during veterinary investigation. Delay in diagnosis impact on potential size of epidemic in time. Normally carrying of clinical sample to the laboratory needs more than 24 hours of time. Rapid test result can support local decision in managing the outbreaks. However there are limitation over the rapid test in comparison to the laboratory test as most

of the test are operated by non-specialist personal, can be carried out on limited number of sample and the assay performances may not be equivalent to laboratory based test.

The different pen side test developed for diagnosis of diseases are based on immunoassay method following principle of lateral flow assay, biosensors and molecular methods like mobile PCR assay, isothermal assay techniques etc. Here in this paper, we will discuss some of the recent development of pen side test in diagnosis of specific diseases.

Development of rapid chromatographic strip-tests for the diagnosis of rinderpest and peste des pet itsruminants viruses

The immune-chromatographic strip is a new technique in which a cellulose membrane is used as the carrier and a colloidal gold labelled antigen or antibody is used as the tracer. This technique has several advantages over traditional immunoassays, such as simplicity of the procedure, rapid operation and immediate results, low cost, no requirements for skilled technicians or expensive equipment (Cui et al., 2008). Because of these characteristics, the immune chromatographic strip test is suitable for on-site detection of antibodies or antigens (Peng et al., 2007).

The development of this rapid chromatographic strip test for pen-side diagnosis of RPV was described by Brüning et al. (1999). In the original paper, several points were made for the improvement of the rapid diagnostic test for RPV including the enhancement of reactivity with RPV of African lineage 2. It was also suggested that the rapid chromatographic strip test technology could be applied to the detection of other diseases of veterinary importance. Since the publication of that paper, a new collaborative link was created with Svanova Biotech for the production of RP and peste des petits ruminants virus (PPRV) specific rapid diagnostic devices. A pen-side diagnostic test for the detection of PPRV in goats and sheep would be beneficial to any control/eradication programme for PPR which, given the success of GREP, should be one of the next targets as envisaged by the FAO (2010). The improvement of the rapid diagnostic test for the detection of RPV and the development of a similar test for the detection of PPRV using lateral flow technology are described by Richardson et al. 2011. In this test using the Svanova Biotech format, a PPRV specific Mab (C77) was used for the development of the PPR test. This Mab recognised a wide range of PPRV isolates and did not show any cross-reactivity with any other virus tested. In animal experiments the device was able to detect viral antigen in eye swabs taken from the animals.

Chromatographic strip test for FMD diagnosis

Chromatographic strip device has been found equivalent sensitivity to ELISA for detection of contemporary virus strains in cell culture supernatant fluids of FMD virus and even more sensitive than ELISA for the diagnosis of all seven serotypes of FMD virus in the epithelial suspensions and nasal swabs (Reid et al 2001). This device detected FMD viral antigen in nasal swabs, epithelial suspensions and probangs from clinical samples from animals infected experimentally and in supernatant fluids resulting from their passage in cell culture.

Again a simple, rapid, colloidal gold-based immuno chromatographic strip tests were developed for easy clinical testing of serotype A of FMDV in field sites was developed with

sensitivity and specificity 88.7% and 98.7%, respectively (Jiang et al 2011). Such pen-side diagnosis would have particular benefits in FMD emergencies

Chromatographic dipstick test for Trichomonas detection

The Xenostrip-Tv test (Xenotope Diagnostics) is a qualitative assay that detects *T. vaginalis*-specific antigen by color immune chromatographic "dipstick" technology with mouse antibodies bound to a nitrocellulose membrane. If *T. vaginalis* is present in a specimen, a specific trichomonad antigen forms a complex with the primary murine anti-trichomonas antibody conjugated to red particles, and the secondary anti-mouse capture antibodies will then bind to the antigen complex. A red test line indicates a positive result. A second capture line, comprising rabbit anti-mouse antibodies, is incorporated into each test strip to capture any excess primary anti-trichomonas antibodies. This also forms a red test line and serves as a positive control, monitoring antibody stability and performance. A red control line but no red test line is a presumptive negative result, and if no red control line appears or background color makes the reading impossible, then the result is invalid. Ten drops of sample buffer (Xenotope Diagnostics) was added to each specimen tube, the absorbent end of a Xenostrip test strip was placed in the tube, and the results were read at 10 min. The results were interpreted as: a red test line indicated a positive result, a red control line but no red test line was a presumptive negative result, and if no red control line appeared or if the test could not be interpreted because of high background color then the result was determined to be invalid. All Xenostrip-Tv test kits were provided by Xenotope Diagnostics. The Xenostrip-Tv test has been licensed to Genzyme Diagnostics, a division of Genzyme General, Cambridge, Mass. Comparison of Xenostrip-Tv, was done to wet mount and PCR for the diagnosis of *Trichomonas vaginalis* infection in women revealed more sensitive than wet mount test. Therefore considered as an alternative to wet mount for point-of-care diagnosis of trichomoniasis, especially in settings where microscopy is impractical (Pillay et al 2004).

Lateral flow device (LFD) for the pen side diagnosis of Foot and Mouth Diseases

The Lateral flow assay (LFA) is an appropriate technology on which to base a rapid assay. The technique permits rapid diagnosis, allowing time for the early implementation of control measures to reduce the possibility of spread of FMD. The LFA has been developed widely to support clinical diagnosis of different diseases (Al-Yousif et al 2002, Kameyama et al 2006), including FMD (Reid et. al. 2001, Ferris et al. 2009). The diagnostic sensitivity of the LFA for FMDV types O, A, C, and Asia 1 was similar, at approximately 87.3%, to that of 87.7% obtained with antigen enzyme-linked immunosorbent assay (Oeam et al 2009). The diagnostic specificity of the LFA was 98.8%, compared to 100% for the Ag-ELISA. The description of the test includes MAb 70-17 to FMDV is conjugated with coloured gold particles and is immobilized as a test line on a membrane. FMDV antigens present in sample bind to the gold particles and form antigen-antibody-gold conjugate complexes, which migrate forward along the membrane. The complexes will be captured by the immobilized MAb 70-17, resulting in a coloured band(s) in the test line. One or two bands are indicators of a positive test result. One band in the control line is significant for a negative test result, as the control antibody will bind the gold conjugate with both positive and negative samples and ensures correct test performance. Recently a lateral flow device (LFD) for the detection of foot-and-mouth disease virus (FMDV) of the SAT 2 serotype was developed using a

monoclonal antibody (Mab 2H6) for providing rapid and objective support to veterinarians in their clinical judgment of the disease and for specific confirmation of a FMDV type SAT 2 infection (Ferris et al 2010). More recently, Morioka et al (2015) developed and evaluated lateral flow strip technology for identifying and distinguishing all FMD serotypes in clinical sample (vesicular fluids, nasal swab, vesicular eruption) and opined that it is highly sensitive and accuracy in serotyping in similar to ELISA and RT-PCR. In such way the technology will be highly useful for detection of FMD where laboratory facilities is not adequate.

Lateral flow devices for the detection of vesicular stomatitis virus in clinical samples

Use of the LFD in diagnosis vesicular stomatitis was described by Bruning et al, 1999 and Ferries et al 2009 previously, and more recently by Ferries et al 2011. Briefly, aliquotsof the epithelial suspensions or cell culture supernatants were mixed with an equal volume of the LFD sample buffer and 200 µlof the mixture was applied to the sample pad of the LFD. If presentin the sample, VSV antigen bound to the type specific Mab coated with latexmicroparticles and formed an immune complex. Following migration along the membrane by capillary action, the complex reached the immobilised Mab in the Test window, resulting inan accumulation of complexes indicated by a blue line visible byeye (if VSV was present in sufficient concentration in the sample)and indicative of a positive result. No band at the test line indicateda negative result. The immobilised anti-mouse immunoglobulins antibody in the control window bound the excess Mab-coatedlatexmicroparticles in both positive and negative samples andensured correct test performance. The test (and control) lines wereobserved for colour development at intervals over a 30 min periodfrom sample addition and reactions scored subjectively from negativeto strong (colour development often occurred within 2–3 minof sample addition of suspensions containing high amounts of VSVantigen) positive.

Multiplex agglutination based of penside diagnostic against FMD virus

Saxena et al 2012 developed a penside diagnostic test based on multiplex agglutination to differentiate serum antibodies against different serotypes of Foot and Mouth Disease (FMD) virus employing inactivated FMDV of serotypes O, A and Asia-1 conjugated with latex beads/microspheres of different colours. Further sensitivity of the test is enhanced by using Antiglobulin through cross-linking of smaller clumps hence multiplex agglutination were found more sensitive minimizing false negative results. Peptide based Latex agglutination test has found very easy, effective and rapid in identifying the serotype of FMD virus (Kaur et al, 2013).

Super agglutination test for diagnosis of Brucella infection

A new agglutination test rather modification of Rose Bengal Plate test for detection of Brucella infection has been developed by Saxena and Kaur (2013) where it is possible to minimize the false negative and false positive generally encountered with common agglutination test. False negative results due to smaller clumps formed by low titre of antibodies in serum are minimized by the addition of biotinylated antiglobulin followed by avidin which forms easily detectable larger clumps. Similarly, prior staining of serum antibodies with a dye helps in differentiating a specific agglutinate formed by both antigen and antibody, from a non-specific aggregate of antigen alone that leads to false positive

results. Superagglutination was found to be more sensitive than the current agglutination tests and agglutination based diagnostic kits (Saxena and Kaur, 2013).

Use of nano particle in diagnosis of Blue tongue in sheep

The use of nanotechnologies for diagnostic application shows great promise to meet rigorous demands of the clinical laboratory for sensitivity and cost-effectiveness. The optical and magnetic properties of the nanoparticles are dependent on its size that can be manipulated to achieve a detectable signal (Salata, 2004). Immunodominant antigenic peptide of blue tongue virus are labelled with gold nano particle and are allowed to interact with tested sera / specific BTV antibodies, they get aggregated resulting in coupling of plasmon–plasmonresonance leading to change in the optical property which can be detected by the colour change on the NCM membrane. The test was termed as Spot test and developed by Saxena et al, 2012 at IVRI, India.

Use of Volatile organic compound detection for diagnosis of infectious diseases

Recently, significant progress has been made in developing tests for rapid diagnosis of disease based on the detection and analysis of volatile organic compounds (VOC) present in clinical samples, such as blood, urine and breath. The principle behind the approach is that clinical specimens from an infected individual produce a volatile chemical signature that is distinguishable from that obtained from uninfected individuals. The inherent advantages of this approach are that multiple markers of infection are examined simultaneously without needing prior knowledge of the underlying biology. These volatile organic compounds can be sensed by using Electronic nose (eNose). eNOSE is the colloquial name for an instrument made up of chemical sensors combined with a pattern recognition system. The key function of an EN is to mimic the human olfactory system. In the EN, the human olfactory receptors have their analogues in chemical sensors that produce an electrical signal (similar to nerve cells). These signals are subsequently analyzed by pattern recognition software.

Differentiation was possible for badgers and cattle with TB from healthy controls by analysing the volatiles present in serum using an electronic nose (Fend et al, 2005). In this study samples obtained from both experimentally infected badgers and cattle, as well as naturally infected badgers. Without exception, the EN was able to discriminate infected animals from controls as early as 3 weeks after infection with M. bovis, the earliest time point examined post-challenge. The EN approach is a straightforward alternative to conventional methods of TB diagnosis, and it offers considerable potential as a sensitive, rapid, and cost-effective means of diagnosing *M. bovis* infection in cattle and badgers. However possibility of detection of VOC marker in urine for diagnosis human TB (Banday et al, 2011) and inflammatory bowel disease (Jayasena et al 2013) is also reported.

Integrated Nano-Technologies has developed a novel DNA-based biosensor that can rapidly and accurately detect and identify pathogenic organisms (Connolly, 2004). The sensor is capable of detecting the binding of a single molecule of DNA or RNA, therefore this system does not require PCR amplification. The biosensor consists of oligonucleotide probes attached to multiple pairs of inter digitated electrodes on a microchip. Hybridisation of target DNA tothe DNA capture probes that are bound to the electro desforms a DNA bridge

connecting the two electrodes. Chemical treatment of the DNA bridge coats it with metal and converts it into a conductive wire. Formation of one metallised DNA bridge reduces the electrical resistance of the sensor 1,000-fold, enabling the detection of a single molecule of DNA. Current research is focused on automation and integration of sample preparation procedures, PCR amplification, and detection into a single microchip or instrument for rapid assays with minimal user-intervention to eliminate the possibility of sample contamination and the need for highly skilled personnel to operate the system. Although these technologies are major improvements on early methods, there are some obvious limitations regarding their performance.

Mobile PCR

The Portable Veterinary Diagnostic Laboratory (Smiths Detection; http://www.smithsdetection.com/vet) comprises a portable briefcase-sized PCR instrument and a disposable sample preparation unit. This integrated system provides rapid on-site identification under a wide range of weather conditions for veterinarians or other workers in animal health. The operators require no technical understanding of the PCR methodology, but the equipment provides a result concerning the suspected diagnosis of a viral disease in the field. The type of sample that can be used is determined by the disease/veterinarian, and both RNA and DNA-based pathogens can be identified with this system. Such systems typically include a global positioning system (GPS) and wireless communications so that data can be sent back to a centralised facility for surveillance or to aid in controlling disease spread during an outbreak.

Recently a single use closed PCR system has been developed, the Cepheid Gene Xpert System (Sunnyvale California) for the diagnosis of *Mycobacterium tuberculosis* complex infections in humans and the identification of antimicrobial multi-resistance using sputum samples (Helb et al. 2010). This test allows for considerable automation with all reagents used for bacterial disruption, nucleic acid extraction, amplification and amplicon detection inside a disposable cartridge. Results are generated within 2hours of processing and to be promising. Test sensitivity evaluation recorded 98.2% in smear positive (microscopy) patients and 72.5% in smear negative patients (Boehme et al. 2010). The test had a sensitivity of 90.3% compared to 67.1%for microscopy in culture positive patients (Boehme et al. 2011). While the test has only been used in humans on sputum samples and no studies have been undertaken in cattle to date these results at least suggest that the possibility of this type of technology may become a useful rapid test in the future for diagnosis of bovine TB in animal samples.

Probes based field diagnosis

Recent advances in molecular biology and more generally in biotechnology may help in development of field diagnostic kits. Probe based biotechnology test is very reliable tools which would enable field veterinarians and/or technicians to obtain a rapid confirmation of clinical diagnoses. Moreover, these field kits could help diagnosticians to make rapid and appropriate decisions in the event of a disease outbreak.

For rinderpest and peste des petits ruminants Complementary deoxyribonucleic acid (cDNA) clones specific for the nucleocapsid genes of the rinderpest and PPR have been used as radio-labelled probes to detect unequivocally these two viruses (Diallo et al, 1989). When this test was performed on lymphocytes from cattle experimentally infected with rinderpest in Chad, it was possible to detect the virus ten days before the onset of disease.

To promote wide use of the probe technology in Africa, efforts were made to develop non-radioactive oligonucleotide probes. Two 20-mer oligonucleotides (specific for the variable 3 end of the N genes) were synthesised and labelled with biotin or digoxigenin. Unfortunately, the use of such probes on biological samples was disappointing: low sensitivity and considerable non-specific background led to unreliable results. However, digoigenin labelled probe has been used for various Mycoplasma *spp* detection.

Diagnosis of respiratory pathogen by Point of Care (POC) test

Debate on use and applicability of POC on respiratory pathogen diagnosis is varied widely; however different manufactures have developed rapid technique for accurate diagnosis of lower respiratory pathogen. (Patrick et al 2007). The POC test for diagnosis of respiratory pathogens mostly have been practised for human cases. However, use of the same in animals can be a promising as most of the respiratory infection in animals are having complex etiological occurrence. A few of them is discussed below.

QuickVue Influenza A + B test

The QuickVue Influenza A + B test (Quidel Corporation, San Diego, Calif, USA) is an enzyme immunoassay that uses monoclonal antibodies against various influenza A and B antigens. The antibodies are impregnated in a test strip. Reagent solution is added to the provided extraction tube, which is then shaken to dissolve the contents. A nasal swab is inserted into the tube and rotated and left for 1 minute before being removed. Alternatively, a dropper is provided that can be used to add fluid from nasal washings or an NPA directly to the extraction tube in place of the nasal swab. The test strip is then inserted into the tube and left for 10 minutes. Influenza virus antigens react with reagents in the test strip, with positive results signified by a pink or red line. Sensitivity is 74%–95% early in the illness, but decreases with each day of illness and possibly also if the test is used after antiviral medications are initiated. Specificity is initially 76%–100%, but decreases if the test is delayed (Pachucki 2005) QuickVue A + B is able to distinguish between influenza A and B viruses.

BinaxNOW Influenza A & B test

The BinaxNOW Influenza A & B test (Binax, Scarborough, Me, USA) is an immunochromatographic test (ICT) that uses monoclonal antibodies bound to a membrane and directed against nucleoproteins of both influenza A and B viruses. It can be used with either an NPA or a nasal swab, but is slightly easier with the former. The test comes as a foldable cardboard card. After obtaining an NPA, a supplied pipette is used to transfer 100 μL onto the white sample pad of the test card. An adhesive liner is removed and the card is then folded over and closed. It is read 15 minutes later. A blue control line at the bottom of the card window should turn pink or purple for the test to be valid. Tests that are positive for

influenza A and B will have a pink or purple line in the middle or upper third of the card window. If a nasal swab is used instead of an NPA, the swab should be placed into a supplied vial of elution solution, rotated vigorously three times and removed. The pipette is then used to transfer some of the elution solution. This reduces the sensitivity of the test slightly.Sensitivity of the test is 62%–82% for influenza A and 58%–71% for influenza B. Specificities are 92%–100% (Cruz et al 2006). This is the simplest of the rapid tests for the person doing the test and, like the QuickVue test, can distinguish between influenza A and B viruses.

BinaxNOW Streptococcus pneumoniae urinary antigen test

The BinaxNOW Streptococcus pneumoniae urinary antigen test (Binax, Scarborough, Me, USA) is a rapid ICT assay performed on standard urine samples. A swab is dipped in the urine and then placed on a nitrocellulose membrane that contains rabbit antibodies against S. pneumoniae. Six drops of a supplied reagent solution are added, and after 15 minutes the card is read. There is one line for the internal control, and the appearance of a second line signifies a positive result. The test detects the C-polysaccharide from the cell wall of all pneumococcal serotypes.The test is useful for diagnosing pneumococcal infections rapidly — particularly in people who have already received antibiotics as, unlike cultures of blood and sputum, antibiotics do not appear to affect the test's accuracy. The test appears to be less useful in children because nasopharyngeal colonisation with S. pneumoniae can lead to false positive results(Dowell et al 2001). Sensitivity is 70%–92% for patients with bacteraemic pneumococcal pneumonia and is at the higher end of the range for those with more severe infection (Smith 2003)

POC for Respiratory Syncytial virus (RSV)

POC Tests for RSV require a nasopharyngeal swab, NPA or nasal washings. These are intended for use in neonatal or paediatric populations and are less accurate when used in adults (Ohm-smith et al 2004). The benefits of such tests are the rapid institution of isolation precautions to reduce nosocomial transmission, a possible reduction in antibiotic use, and the option of using specific antiviral therapy such as ribavirin (Zheng et al 2004) The simplest test is the BinaxNOW RSV test (Binax, Scarborough, Me, USA), which is performed in the same way as the BinaxNOW influenza test.

Paper based multifluidic device

Traditional POC paper-based devices (i.e. lateral flow devices) can run more than one test in series which require that the tests be compatible with each other in terms of buffers and reagents and there should not be any cross reactivity between the assays. Paper-based microfluidic devices consist of hydrophilic paper channels defined by patterning of hydrophobic barriers or by cutting the material. The test directs fluid towards specific detection zones and in 3 dimensions which performs operations such as mixing, splitting and filtration automatically. It allows multiplexing of a small sample volume (<40 µl) in independent assays done in parallel with no worry about cross-reactivity. These assays are portable and disposable. Proof-of-principle studies have tested the ability to conduct clinical chemistry, enzymatic, immunoassay and enzyme-linked immunosorbent assays. Pollock et al (2012) developed a test for monitoring liver function for patients with liver disease or those

taking medications with hepatotoxicity. This POC assay was found rapid, semi quantitative measurement of AST and ALT from a finger stick whole blood specimen.

Programmable Bio-Nanochip (P-BNC) technology

The technology provides the ability to rapidly secure sensitive, reliable simultaneous measurements of key biomarkers at the POC. A sensor can function as a standard platform that can serve multiple applications by inserting a molecular level "code" which is biomarker specific reagents. The definition of Bio refers the capacity to measure and extract the bio-signatures associated with disease progression; Nano refers the capacity to miniaturize the system through use of nano-nets for capture and quantum dots for increased signal generation and Chip denotes the capacity to mass-produce sensor elements similar to microchips, that leads to high performance at low cost.

Based on this principle of bio nanochip for cardiovascular diseases CVD diagnosis has been developed by Christodoulides et al. (2012), where saliva was used to identify biomarker of acute myocardial infarction (AMI). It was able to measure of 21 proteins in AMI patients and healthy control.

Point of care compatible Nucleic acid testing (NAT) has increased during recent years to get more accuracy in POC diagnosis in terms of detection by nucleic acid. The application of NAT for diagnosis of infant HIV (Leelawiwat et al 2009), Groub B streptococcus in vaginal tract(De Tejada et al, 2011) and for Tuberculosis (Blakemore et al , 2010) are possible and some of the test has already been approved by WHO.

CONCLUSIONS

Penside test is a reliable, precise and rapid diagnostics test employed for diagnosis of various infectious diseases. However the sensitivity and specificity of these test varied on different factors like respective microorganisms, environment, temperatures, doses etc etc. The diagnostic tests can be employed in pen side as well for getting a first-hand screening of the herd about the suspected infections. One potential solution is to use rapid POCTs to identify the causative pathogen, such that either no antibacterials are needed (eg, in the case of viral infection) or patients can be safely treated with cheap, narrow-spectrum agents. Use of pen side diagnosis is helpful in differentiating the potential infection in animal from vaccinated one as in PPR, RP FMD etc. Cross reactivity is one of the major drawback in these tests and which may give false positive or false negative results.

REFERENCES

Banday, K.M., Pasikanti, K.K., Chan, E.C., Singla, R., Rao, K.V., Chauhan, V.S., Nanda, R.K., 2011. Use of urine volatile organic compound to discriminate tuberculosis patients from healthy subject. Anal chemistry15, 5526-34.

Blakemore, R., Story, E., Helb, D., Kop, J., Banada, P., Owens, M.R., Chakravorty, S., Jones, M., Alland, D., 2010. Evaluation of the analytical performance of the Xpert MTB/RIF assay. J Clin Microbiol. 48, 2495–2501,

Boehme, C.C., Nicol, M.P., Nabeta, P., Michael, J.S., Gotuzzo, E., Tahirli, R., Gler, M.T., 2011. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. The Lancet 377, 1495-1505.

Brüning, A., Bellamy, K., Talbot, D., Anderson, J., 1999. A rapid chromatographic strip test for the pen-side diagnosis of rinderpest virus. J. Virol. Methods 81, 143–154.

Christodoulides, N., Pierre, F.N, McDevitt, J.T., 2012. Programmable Bio-Nano-Chip Technology for the Diagnosis of Cardiovascular Disease at the Point-of-Care, Methodist Debakey Cardiovasc J. 8, 6-12.

Connolly, M., Chafin, D., Hill, D., 2004. Development of a fieldable, rapid, accurate and sensitive bio-electronic DNAbiosensor. Proc. 24th Army Science Conference. Available at:http://en.scientificcommons.org/19926834.

Cui, S., Zhou, S., Chen, C., Qi, T., Zhang, C., Oh, J., 2008. A simple and rapid immunochromatographic strip test for detecting antibody to porcine reproductive and respiratory syndrome virus. J. Virol. Met. 152, 38–42.

Cruz, A.T., Cazacu, A.C., McBride, L.J, 2006. Performance characteristics of a rapid immunochromatographic assay for detection of influenza virus in children during the 2003 to 2004 influenza season. Ann Emerg Med. 47: 250-254.

De Tejada, B.M., Pfister, R.E., Renzi, G., Francois, P., Irion, O., Boulvain, M., Schrenzel, J., 2011. Intrapartum group B streptococcus detection by rapid polymerase chain reaction assay for the prevention of neonatal sepsis. Clin Microbiol Infect. 17, 1786-91.

Diallo, A., Barrett, T., Barbron, M., Subbarao, S.M., Taylor, W.P., 1989. Differentiation of rinderpest and peste des petits ruminants viruses using specific cDNA clones. J. virol. Meth., 23, 127-136.

Dowell, S.F., Garman, R.L., Liu, G., 2001. Evaluation of Binax NOW, an assay for the detection of pneumococcal antigen in urine samples, performed among pediatric patients. Clin Infect Dis 32: 824-825

Fend, R., Geddes, R., Lesellier, S., Vordermeier, H.M. 2005. Use of an Electric Nose to diagnose Mycobacterium bovis infection in Badgers and Cattle. J Clin Microbiol 43, 1745-51.

Ferris, N.P., Clavijo, A., Yang, M., Velazquez-Salinas, L., Nordengrahn, A., Hutchings, G.H, Kristersson, T., Merzad, M. 2012. Development and laboratory evaluation of two lateral flow devices for the detection of vesicular stomatitis virus in clinical samples. J Virological Method 180, 96-100.

Helb, D., Jones, M., Story, E., Boehme, C., Wallace, E., Ho, K., Kop, J., Owens,M.R., 2010. Rapid detection of *Mycobacterium tuberculosis* and Rifampin resistance by use of on-demand, Near-Patient Technology. J. Clin. Microbiol. 48, 229-237.

Jayasana, H., Khalid, T. Probert, C.S., 2013. PTU-077 Diagnostic potential of volatile organic compounds as urine Biomarkers in Inflammatory Bowel Disease. Gut 62, A76-A77.

Kaur, D., Kaur, G., Chandra, M., Saxena, H.M., Dwivedi, P.M., 2013. Development of a peptide based latex agglutination assay for serotype identification of foot and mouth disease virus. Ind J Exp Biology. 51, 124-128.

Klein, M., Chaefsky, S., Muller, M., 1966. A rapid agglutination test for the detection of antibodies to viruses of influenza. J Immunol 97, 131-137.

Leelawiwat, W., Young, N.L., Chaowanachan, T., Ou, C., Culnane, M, Vanprapa, N., Waranawat, N., Wasinrapee, P., Mock, P.A., Tappero, J., 2009. Dried blood spots for the diagnosis and quantitation of HIV-1: stability studies and evaluation of sensitivity and specificity for the diagnosis of infant HIV-1 infection in Thailand. J Virol Methods. 155, 109–117.

.

Montoya, P.J,, Lukehart, S.A, Brentlinger, P.E., Blanco, A.J., Floriano, F., Sairosse, J., Glovd, S., 2006. Comparison of the diagnostic accuracy of a rapid immuno chromatographic test and the rapid plasma reagin test for antenatal syphilis screening in Mozambique. Bull World Health Organ. 84, 97–104.

Morioka, K., Fukai, K., Yoshida, K., Kitano, R., Yamazoe, R., Yamada, M., Nishi, T., Kanno, T., 2015. Development and Evaluation of a Rapid Antigen Detection and Serotyping Lateral Flow Antigen Detection System for Foot-and-Mouth Disease Virus. PLoS ONE 10 (8): e0134931. doi:10.1371/journal.pone.0134931

Oem, J.K., Ferris, N.P., Lee, K.N., Joo, Y.S., Hyun, B.H., Park, J.H. 2009. Simple and Rapid Lateral-Flow Assay for the Detection of Foot-and-Mouth Disease Virus. Clin Vacc Immunol. 16, 1660-1664.

Ohm-Smith, M.J., Nassos, P.S., Haller, B.L., 2004. Evaluation of the Binax NOW, BD Directigen, and BD Directigen EZ assays for detection of respiratory syncytial virus. J Clin Microbiol. 42, 2996-2999.

Opekun, A.R., Luu, P., Gotschall, A.B., Abdalla, N., Torres, E., Rudd, S.B., Graham, D.Y., 2006. Point-of-care Helicobacter pylori urine antibody detection in a multi-ethnic adult population in the United States. Transl Res. 148, 13-18.

Pachucki, C.T. 2005. Rapid test for influenza. Curr. Infect Dis Resp. 7, 187-192.

Patrick, G.P., Charles, Grayson, M.L., 2007. Point of care test for lower respiratory tract infections. Med J Aust. 187, 36-39.

Peeling, R.W., Mabey, D. 2010. Point-of-care tests for diagnosing infections in the developing world. Clin Microbiol Infect. 16, 1062–1069.

Peng, D., Hu, S., Hua, Y., Xiao, Y., Li, Z., Wang, X., Bi, D., 2007. Comparison of a new gold immune chromatographic assay for the detection of antibodies against avian influenza virus with hemagglutination inhibition and agar gel immunodiffusion assays. Vet. Immunol Immunopathol. 117, 17–25.

Pillay, A., Lewis, J., Ballard, R.C., 2004. Evaluation of Xenostrip-Tv, a rapid diagnostic test for Trichomonasvaginalis infection. J Clin Micrbiol. 42, 3853-3856.

Pollock, N.R., Rolland, J.P., Kumar, S., Beattie, P.D., Jain, S., Noubary, F., Whitesides, G.M., 2012. A paper based multiplexed transaminase test for low cost point of care liver function testing. Sci Transl med. 4, 152ra129. scitransalmed.3003981.

Reid, S.M., Ferris, N.P., Bruning, A., Hutchings, G.H., Kowalska, Z., Akerblom, L., 2001. Development of a rapid chromatographic strip test for pen side detection of foot and mouth disease virus antigen. J Virological methods. 96, 189-202.

Richardson, A.B., Akerblom, L., Kingeborn, B.. Anderson, J., 2011. Improvement and development of rapid chromatographic strip-tests for the diagnosis of rinderpest and peste des petitsruminants viruses. J Virological Methods. 174, 42–46.

Saxena, H.M., Kaur, P., 2013. A new superagglutination test to minimize false negative and false positive results common with plate/slide agglutination tests for the diagnosis of infectious diseases. Int. J. Trop. Dis. Health. 3,199–209.

Saxena H.M., Kaur, P., Chandra, M., 2012. A new pen side diagnostic kit for simultaneous detection of Antibodies to different serotype of Foot and Mouth disease virus in sera. J Viro Microbiol. Article ID 660259, 39 minipages DOI: 10.5171/2012.660259.

Saxena, V.K., Deb, R., Srivastava., S., Kantaraja, C., Kumar, A., Kumar, S., 2012. Functionalizing gold nanoparticles with bluetongue virus multiple peptide antigens utilizing gold–thiol interaction: A novel approach to develop pen side test. Res. Vet. Sci. 93, 1531-1536.

Smith, M.D., Derrington, P., Evans, R., Creek, M., Morris, R., Dance A.B.D., Cartwright, K., 2003. Rapid diagnosis of bacteremic pneumococcal infections in adults by using the Binax NOW Streptococcus pneumoniae urinary antigen test: a prospective, controlled clinical evaluation. J Clin Microbiol. 41, 2810-2813.

Zheng, X., Quianzon, S., Mu, Y., Katz, B.Z., 2004. Comparison of two new rapid antigen detection assays for respiratory syncytial virus with another assay and shell vial culture. J ClinVirol. 31, 130-133.

Zijlstra, E.E., Osman, O.F., Hofland, H.W., Oskam, L., Ghalib, H.W., el-Haasan, A.M., Kager, P.A., Meredith, S.E., 1997. The direct agglutination test for diagnosis of visceral leishmaniasis under field condition in Sudan: comparison of aquous and freeze dried antigen. Trans R Sco. Trop Med. Hyg. 91, 671-673.