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Review on Recent Advances in Nanotechnology Based Diagnostic Tools for Infectious Disease

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ABSTRACT:
One of the main causes of morbidity and mortality in the developing world is infectious diseases, which are common there. Because it is so easy to travel from one part of the world to another, infectious diseases can start in a confined area and spread quickly at any time. This might cause a worldwide pandemic. One essential to limiting this spread is the development of diagnostics that can quickly identify the infectious agent so that one may properly treat or in some severe circumstances, isolate a patient. Although diagnostic technologies have advanced significantly, infectious disease diagnostics are still based on outdated technology from the 1950s, which has limitations such as slow processing speed, the requirement for specialized personnel, a low detection threshold, and the inability to identify several infectious agent strains. Here, we outline developments in infectious disease diagnostics using nanotechnology and microtechnology. Nanomaterials serve as labels or barcodes in these diagnostic techniques, while microfluidic technologies automate the sample the assays and their preparation. We outline the difficulties and current status of the field.

INTRODUCTION:

Despite major advancements in diagnostics and medications during the past century, infectious diseases brought on by bacteria (tuberculosis and other diseases), parasites (malaria, trypanosomiasis, and leishmaniasis), and viruses (HIV, hepatitis C, and dengue fever) In the poor world, cholera is one of the leading causes of sickness and mortality. Globalization and international travel can cause infectious disease outbreaks to spread quickly throughout the world, even though they may start off locally. For instance. Researchers and physicians need precise technologies for pathogen identification in order to evaluate the severity of a patient's condition, recommend appropriate therapy, and in certain situations, isolate infected individuals in order to stop the spread of infectious diseases. Diagnostics for infectious diseases have not improved much over the past 50 years, despite the significance of accurate diagnosis. Gold standard methods Microscopy, tissue culture, lateral flow immunoassays (sometimes called dipsticks or immunochromatographic tests, or ICTs), and enzyme-linked immunosorbent assays (ELISA) are among the diagnostic techniques used in infectious diseases. These methods are sluggish, have a low detection threshold, are costly, and have a limited capacity to distinguish between several diseases. The polymerase chain reaction (PCR) method has recently been modified and applied to the identification of pathogens. PCR can distinguish between various pathogen strains and has a greater detection threshold than earlier methods (for example, it is one million times more sensitive than

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lateral flow immunoassays). However, the same issues that plague the most widely used diagnostic methods also limit PCR and real-time PCR.

Despite being widely utilized in the developed world, these diagnostic tools are frequently ill-suited for the developing world, where infectious illnesses are a leading cause of morbidity and mortality as well as areas with potentially limited access to healthcare and laboratory facilities. As a result, the developing globe poses new diagnostic engineering issues. A portable, affordable, point-of-source or point-of-care detection system that is highly sensitive, accurate, and capable of differentiating between several pathogens would be the ideal diagnostic tool for the developing world.

The primary design principles for creating infectious disease diagnostics have been emphasized by the World Health Organization. The latest advancements in molecular diagnostics based on nanotechnology are the main topic of this review paper. These new technologies have the potential to overcome several of the technical difficulties related to the diagnosis of infectious diseases in impoverished nations. In order to illustrate the present norms and constraints in infectious disease detection, we will utilize a number of the most urgent infectious diseases in the developing world as examples in the first section of the review paper. Next, with an emphasis on technologies related to infectious diseases, we outline the ongoing research initiatives in nanotechnology-based molecular diagnostics.

1.1. Diagnostics for bacterial tuberculosis

Mycobacterium tuberculosis is the causative agent of tuberculosis. Although extrapulmonary tuberculosis can potentially develop in the central nervous or circulatory systems, or away, the illness primarily manifests in the lungs. within the body. When someone with tuberculosis coughs, clusters of bacilli are released into the air, where they're gobbled by those in close propinquity. The bacilli are taken up by macrophages in the lungs, where they may be excluded. But bacilli can also lie dormant in lung towel, a condition called idle infection. A dormant infection may come an active complaint due to an environmental detector, similar as gestation, a posterior infection with another pathogen, or vulnerable system weakness. The death rate from undressed active TB is over 50.

Chest radiography is used to diagnose active TB, and sputum collection and microbiological culture are sometimes performed after the diagnosis. Due to its limited sensitivity, radiological testing necessitates skilled personnel to operate the imaging apparatus. Typically, tuberculosis cultures are more the microbiological test depends on bacterial growth and can take weeks to produce a definitive result, but it is more sensitive than chest radiology. Growing the cultures requires a level 3 biosafety lab because tuberculosis is contagious. Such diagnostic methods are therefore unsuitable for the poor world due to these criteria. Diagnosing latent tuberculosis is considerably more difficult because it lacks the usual symptoms, such as fever, coughing, sputum production, etc.

The current accepted test for tuberculin is the tuberculin skin test (TST). latent infection. The pure protein derivative (PPD), a combination of more than 200 TB antigens, is used in this test to gauge a person's immune response. An induration, or localized inflammation, forms on the forearm where the antigens were subcutaneously injected in those who have previously been exposed to the pathogen (such as through a latent infection). The test is non-invasive and reasonably priced, but it necessitates two clinic visits within a given time frame. Additionally, the test frequently produces false-negative results in patients who have already received the Bacillus Calmette-Gurin (BCG) vaccine and false-positive results in patients co-infected with HIV who have low T-cell counts.

1.2. Diagnostics for the human immunodeficiency virus

At the moment, a Western blot after an enzyme immunoassay (EIA) is the gold standard for HIV detection. IgG antibodies were detected by first-generation EIAs, but third-generation EIAs currently detect IgM antibodies are generated in reaction to HIV. Two clinical visits are necessary for these tests: one to provide a blood sample, and another to obtain the findings. Trained laboratory

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(2), 1737-1743 | ISSN:2251-6727

staff are also needed. For the detection of HIV antibodies, rapid point-of-care tests (POCT) are available and offer comparable sensitivity (98%–100%) and specificity (86%–100%) to conventional enzyme immunoassays, with an outlier at 75%. However, IgG or IgM anti-HIV antibodies (made in reaction to the infection) may only be detected by Western blots 3–6 weeks after infection, while viral RNA can be directly detected 9 days after infection.

1.3. Diagnostics for malaria parasites

Plasmodium falciparum is the most lethal of the protozoan parasites that cause malaria, while P. vivax, P. malariae, and P. ovale are less serious. Anophelene is the vector of malaria transmission. mosquitoes in tropical areas, and it poses the greatest risk to pregnant women due to the reversible loss of immunity during pregnancy, as well as to infants, whose immune systems are still developing and underdeveloped. The illness affects both the liver and red blood cells, and it might resurface after many years due to a latent phase in the liver. There are several anti-malarial medications on the market, but because the best anti-malarials are sometimes given without a correct diagnosis, drug resistance has grown to be a serious issue. Even though many other diseases present similarly, many patients in developing countries are now treated based only on their symptoms.

The gold standard for detecting malaria is microscopy. However, many strains may exist in the same host, and microscopic identification necessitates highly skilled and experienced personnel. Morphological The four pertinent Plasmodium species can be distinguished using microscopy, however this depends on experimental methodology and even how antimalarial medications affect strain appearance. To visualize the parasite under light microscopy, a drop of blood from a finger prick is fixed with methanol on a glass slide and stained with dyes. Microscopy, however, has several difficulties. It is frequently difficult to detect parasitemia at low levels, and the analysis calls for highly skilled and experienced personnel.

1.4. Other critical infectious diseases

Even while HIV, malaria, and tuberculosis are major pathogenic risks in the developing world today, other infectious illnesses are also contributing significantly to morbidity and mortality. These alleged African trypanosomiasis, Chagas disease, leishmaniasis, dengue fever, schistosomiasis, diphtheria, influenza, measles, cholera, and leprosy are among the neglected diseases. For these illnesses, rapid POCT would increase access to care in locations with limited resources and enable physicians to treat and isolate patients efficiently without requiring costly laboratory facilities or follow-up visits. Reducing pathogen spread and lowering morbidity and mortality might be possible with the ability to accurately identify and distinguish between diseases that have similar symptoms.

2. NANOTECHNOLOGY DIAGNOSTICS FOR INFECTIOUS DISEASES

Furthermore, to enhance nanostructure monodispersed or lessen non-specific binding of biological or environmental pollutants, nanostructure surfaces can be altered with polymers or other functional groups. (for instance, serum proteins). In order to enable nanoparticles to target a specific gene, protein, cell, or organ in vivo, surfaces can also be altered using molecules like aptamers, peptides, or antibodies. To now, scientists have mostly used nanostructures in cancer applications, where they can serve as imaging probes, cancer medication delivery systems, and tumour cell elimination therapies. The creation of molecular diagnostic platforms based on nanotechnology is a key area of attention for present and future nanotechnology research.

2.1. Simple nanotechnology-based diagnostics

Three distinct platforms for basic infectious disease diagnostics have employed nanomaterials to build sensors:

(1) nanoparticle labels in ICT assays,

(2) nanoparticle aggregation assays, and

Journal of Chemical Health Risks
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(3) nanoparticle complete pathogen labels.
The initial platform's guiding principles—ICT assays—are explained. These assays identify antibodies in blood or other bodily fluids and are based on the same principles as ELISA. Conventional lateral flow assays use dyes, latex particles, or tiny gold nanoparticles as contrast agents to achieve colorimetric detection that is visible to the naked eye. One of the earliest uses of nanoparticles in illness diagnosis was in lateral flow studies, when gold nanoparticles were employed. Depending on the pathogen type, detection limits can vary.

2.2. Multiplexed detection with nano-diagnostics
Although the sensitivity of basic diagnostic platforms based on nanotechnology is comparable to that of gold-standard infectious disease diagnostics, there is limited capacity to screen for numerous pathogens or indicators at once. Plasmodium and other pathogens There are various strains of HIV and parasites, and being able to identify the strain could increase the effectiveness of treatment. Nowadays, creating multiplexed assay systems that can concurrently detect a large number of molecules or entire viruses or bacteria is a primary focus of nanotechnology research. Although there are many different kinds of barcodes, we will concentrate on quantum dot barcodes and the genomic bio-barcode assay (BCA) as an illustration of how barcodes are made and used in infectious diseases. diagnosis of disease. The diagnostic concept is the same for all barcodes based on nanotechnology. Bright, photostable fluorescent markers, semiconductor quantum dots (QDs) have found application in nucleic acid and proteome detection systems. Chan and colleagues created QD barcodes for the multiplexed and high-throughput detection of biomarkers that code for the blood-borne infectious disease using a homogeneous, solution-based test. illnesses (HIV, hepatitis C, and hepatitis B) .
The researchers used two color (570 nm and 615 nm emission) ZnS capped CdSe QDs to construct three barcodes that were coupled with the pathogen biomarkers HIV glycoprotein 41 (gp41) for HIV, HBV surface antigen (HBsAg) for HBV, and HCV non-structural protein 4 (NSP-4) for HCV. Even if PCR sensitivity levels are provided by gold nanoparticle-based BCA tests in conjunction with scanometric detection, a single experiment still takes about six hours.
Because of the long process, there are still practical obstacles to overcome before this chip-based test can be used for quick point-of-care diagnostics. Although these multiplexed detection systems based on nanoparticles offer a lot of promise, they are still somewhat complicated and need a lot of lab equipment.
These technologies might become viable for the developing countries with commercialization and additional research and development. Future research should focus on two key areas: reducing system complexity and integrating the detection strategy into a completely closed diagnostic "black box" that a sample might be inserted into.

2.3. Advanced platforms and read-out systems
Although using nanotechnology alone (such as particle aggregation-based gold nanoparticle tests) shows promise, self-contained platforms for sample processing and read-out analysis are also necessary for nanotechnology diagnostics. In light of this, significant recent Research has demonstrated that microfluidic channels with cross-sectional dimensions ranging from tens to hundreds of microns can be used for nanotechnology research. These lab-on-a-chip (LOC) systems have several benefits, such as shorter analysis times, lower waste creation via downsizing, smaller sample sizes, and less reagent use. time, and more significantly, the possibility of integrating the system with detecting tools to produce portable electronics.
LOC methods offer a crucial bridging technology and could be the best means of delivering diagnostics for nanotechnology. You may read some great reviews on LOC systems to learn more about this technology. Using a single silicon-glass microchamber, another study created a diagnostic DNA assay that could thermally lyse cells, separate genomic DNA using magnetic particles, amplify DNA using PCR, and detect deposited silver electrochemically. E. Coli and Bacillus subtilis

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 1737-1743 | ISSN:2251-6727

pathogens were used as model analytes to illustrate multiplexed detection. Prostate-specific antigen has been detected using the very sensitive BCA assay described in the previous section, which has also been developed for microfluidic applications. Both assay phases could be integrated thanks to a small microfluidic chip. The antigen target was identified by magnetic nanoparticles, which were then rendered immobile by a magnetic field. After that, barcode DNA and antibody-containing gold nanoparticles were introduced and joined to the antigen.

CONLUSION:

Every year, infectious diseases claim millions of lives worldwide, particularly in developing nations. Targeted treatments and other appropriate interventions are essential, and they can only be implemented with context-relevant diagnostics, which are capable of efficiently and economically identifying affected individuals. Nanotechnology may be a key component of the innovative technologies required to create breakthroughs and enable quick, multiplexed disease detection. Promising diagnostic alternatives are already being developed through the use of metallic nanostructures, quantum dots, and other nanoparticles, as well as their integration with lab-on-a-chip technology.

We have talked about several recent developments, such as lab-on-a-chip platforms, multiplexed homogeneous and heterogeneous systems, and extremely sensitive nanoparticle testing. But there are a lot of issues that need to be resolved before diagnostics using nanotechnology are genuinely prepared for application in underdeveloped nations. To increase the specificity of nanotechnology-based detection platforms and enable strain discrimination, these include the identification and selection of efficient antigen, antibody, and nucleotide targets. In order to compare studies of detection limits, universal standards for the evaluation of tests and detection levels must be established. Furthermore, there needs to be ongoing work done to develop smaller detection platforms.

Techniques that streamline purification and separate genes of interest are crucial for genomic detection. Particular facets of nanotechnology research need to be created for the three critical diseases that have been recognized. Rapid multiplexed testing are required for TB in order to identify concurrent HIV infections, and the sensitivity of nanotechnology assays must be utilized in order to identify latent infections. Exceptionally quick HIV detection, ideally based on viral RNA, would help stop the virus's transmission, and therapy would be aided by understanding the viral load.

Lastly, multiplexed detection of other diseases with similar presentations and strain distinction for malaria would allow for focused treatment and stop the growth of parasites resistant to anti-malarial drugs. Despite the fact that infectious illness detection in developing nations has not yet fully benefited from nanotechnology advancements, many of the issues listed by the WHO.

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