NANOTECHNOLOGY AND THE DIAGNOSIS OF TYPHOID FEVER

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For effective management of typhoid, diagnosis of the disease must be done with speed and accuracy. Laboratory diagnosis of typhoid fever requires isolation and identification of Salmonella enterica serotype Typhi. In many areas where the disease is endemic, laboratory capability is limited. Recent advances in molecular immunology have led to the identification of sensitive and specific markers. Currently, alternative methods for biological molecular analysis are enzyme immunoassay, surface plasmon resonance and electrochemical immunoassay. With the development of nanotechnology, various nanoparticles and nano-quantum dots have been used as labels to enhance the sensitivity of the electrochemical immunoassay technique.

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1. Introduction

Typhoid fever remains a serious health problem in many regions of the world. The major causes of typhoid fever are caused by Salmonella enterica serovar Typhi (S. Typhi) and also, to a lesser extent, strains of S. enterica belonging to serovars Paratyphi (S. Paratyphi) A, B and C. This is a highly adapted, human-specific pathogen occurring more frequently in underdeveloped regions of the world where overcrowding and poor sanitation are prevalent.

According to the best global estimates, there are at least 16 million new cases of typhoid fever each year, with 6,000,000 deaths [1]. Between 1-5% of patients with acute typhoid infection have been reported to become chronic carriers of the infection; depending on age, sex and treatment regimen. Furthermore, this chronic carrier state has also been implicated in causation of carcinoma of the gall bladder.

The diagnosis of typhoid fever on clinical grounds is difficult, as the presenting symptoms are diverse [2] and similar to those observed with other common febrile illness, such as malaria and non-severe dengue fever.

The isolation of serotype Typhi from blood remains the method of choice for the laboratory diagnosis [3]. Classical methods are usually used to detect S. typhi, including culturing [4, 5], serological methods, such as slide agglutination and the Widal test [6], and polymerase chain reaction (PCR) [7,8]. Even though these methods can provide highly sensitive results for both qualitative and quantitative analysis, they are quite hard- and time-consuming to perform.

With the above-mentioned drawbacks, efforts to develop a method for S. typhi determination with increased sensitivity and selectivity and a reduction in analysis time needs to be proposed. Currently, alternative methods for biological molecular analysis are enzyme immunoassay [9, 10], surface plasmon resonance [11], and electrochemical immunoassay [12–14]. In particular, the use of electrochemical immunoassay has attracted considerable interest for S.
typhi determination because of its inherent simplicity, high sensitivity, inexpensive instrumentation, and miniaturization.

With the development of nanotechnology, various nanoparticles \cite{15, 16} and nano-quantum dots \cite{17, 18} have been used as labels to enhance the sensitivity of the electrochemical immunoassay technique.

Recently, copper, silver, and gold-enhanced colloidal gold have been reported for immunoglobulin G (IgG) determination, which is the model of electrochemical immunoassay with low detection limits ranged from 1.0 ng/mL to 0.25 pg/mL \cite{19–21}. The metal-enhanced colloidal gold electrochemical stripping metalloimmunoassay combines the high sensitivity of stripping metal analysis with the remarkable signal amplification resulting from the catalytic precipitation of metals onto the gold nanoparticles \cite{21–23}.

4. Conclusions

Nanotechnology is an emerging field that is potentially changing the way we treat and diagnose diseases. The metal-enhanced colloidal gold has not been previously applied to the detection of bacterial cells in real samples, especially for the detection of \textit{S. typhi}. Therefore, one can employ the electrochemical stripping-metallo-immunoassay based on a copper, silver or gold-enhanced – colloidal gold nanoparticle label for the determination of \textit{S. typhi} in real samples, which will be useful in the diagnosis, follow-up treatment, and controlling in advance the epidemic disease of typhoid fever. The coupling of gold nanoparticles with the advantages of electrochemical stripping analysis can easily be extended for detecting other bacterial cells in real samples with high accuracy and sensitivity.

As someone has truly predicted, there has been plenty of room at the bottom to modify and enhance existing technologies by controlling material properties at the nanoscale. Therefore, with sufficient time and research, the promise of nanotechnology based disease diagnosis may become a reality.

References

Typhoid Fever - Etiology, pathophysiology, symptoms, signs, diagnosis & prognosis from the MSD Manuals - Medical Professional Version.

Late in the disease, when intestinal lesions are most prominent, florid diarrhea may occur, and the stool may contain blood (occult in 20% of patients, gross in 10%). In about 2% of patients, severe bleeding occurs during the 3rd week, with a mortality rate of about 25%. An acute abdomen and leukocytosis during the 3rd week may suggest intestinal perforation, which usually involves the distal ileum and occurs in 1 to 2% of patients. Pneumonia may develop during the 2nd or 3rd week and may be due to secondary pneumococcal infection, although S. Typhi itself can also cause pneumonia. The diagnosis of typhoid fever on clinical grounds is difficult, because symptoms are many and similar to those of other common febrile disease, such as malaria and non-severe dengue fever [5]. Although the isolation of Salmonella typhi from the bone marrow is the reference method to confirm a case of typhoid fever, blood culture is more often used as a much more convenient alternative [6]. However, because of the availability period of results (2-3 days) the diagnosis may be delayed or neglected and patients without typhoid fever may receive an unnecessary and inappropriate antibiotic treatment.

Complicated disease: Acute typhoid fever may be severe. Depending on the clinical setting and the quality of available medical care, up to 10% of typhoid patients may develop serious complications. Since the gut-associated lymphoid tissue exhibits prominent pathology, the presence of occult blood is a common finding in the stool of 10-20% of patients, and up to 3% may have melena.

The diagnosis, treatment and prevention of typhoid fever. coagulation, thrombocytopenia and haemolytic uraemic syndrome. In the pre-antibiotic era, which had a different clinical picture, if patients did not die with peritonitis or intestinal haemorrhage, 15% of typhoid fever cases died with prolonged persistent fever and diseases for no clear reason. Typhoid fever is highly contagious. An infected person can pass the bacteria out of their body in their poo (stools) or, less commonly, in their pee (urine). If someone else eats food or drinks water that's been contaminated with a small amount of infected poo or urine, they can become infected with the bacteria and develop typhoid fever. Read more about the causes of typhoid fever. Who's affected? If typhoid fever isn't treated, the symptoms will continue to get worse over the following weeks and the risk of developing potentially fatal complications will increase. Read more about the symptoms of typhoid fever and the complications of typhoid fever. How typhoid fever is treated. Typhoid fever requires prompt treatment with antibiotics.