A Clinical Study of Nucleic Acid Time-of-Flight Mass Spectrometry-Based Analysis of Microorganisms in the Reproductive Tract in Infertility

Informed Consent Form - Informed Notice Page (Study Profile)

Information Leaflet for Informed Consent

Dear Subjects.

Please read this informed consent form carefully and make a careful decision about whether to consent to the storage and future use of your biological samples. We encourage you to have a full discussion with your family and friends before making a decision to participate in this study. You can decide for yourself whether your sample can be stored, for how long, whether it needs to be kept anonymous, and what future studies it can be used for. This informed consent form contains the following two sections.

-Information for subjects (explains information about the biological sample to you)

-Signature page (to record your consent)

Information for Subjects

1. Background, significance and purpose of the study

Mycoplasma, Chlamydia, and gonococcal infections of the female lower genital tract can lead to infertility and a variety of adverse pregnancy outcomes. Lower genital tract bacterial community status types (CST) are closely associated with reproductive tract infections and reproductive health, but there is a lack of a rapid, accurate, stable, and cost-effective clinical assay for both these pathogens and CST, and therefore a lack of assessment of the association of each pathogen infection with CST. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) is more stable and accurate than traditional detection methods such as culture and staining, and can detect multiple microorganisms and their subtypes simultaneously, while it is faster and more economical than high-throughput sequencing methods, and is suitable for the combined detection of multiple microorganisms in clinical settings. The group has already established a comprehensive MALDI-TOF MS platform and put it into clinical testing. This project will establish a new rapid microbiological test for the lower reproductive tract based on MALDI-TOF MS, and use the test developed in this project to test the microecology of the lower reproductive tract of infertile patients and healthy women and to initially analyze their pathogenic infections and CST status. This project will address the practical needs of clinicians for a comprehensive assessment of CST and common pathogenic infections in the female lower genital tract and fill the current technical gap in microbiological testing of the lower genital tract.

This study is to be conducted at Shenzhen Second People's Hospital and is expected to collect cases. We are inviting you to participate in this scientific research project by

collecting/collecting/or keeping your vaginal and cervical secretion samples.

The objectives of this study were 1) to develop a rapid detection method for microorganisms in the lower genital tract based on time-of-flight mass spectrometry (MALDI-TOF MS) for simultaneous detection of multiple pathogens and CST and to evaluate its robustness, and 2) to evaluate the correlation between pathogenic infections in the lower genital tract, CST and infertility using the newly developed assay.

This study has been approved by the Research Ethics Committee of the Shenzhen Second People's Hospital. The Research Ethics Committee of Shenzhen Second People's Hospital has considered that this study is in compliance with the principles of the Declaration of Helsinki, the Civil Code and domestic medical ethics-related laws and regulations and normative guidelines, and meets the requirements of medical ethics.

2. Purpose of collecting samples

Your sample will be used in the study of the association between lower reproductive tract microbes and infertility, and the use of your sample in research related to lower reproductive tract microbes will facilitate the search for effective treatment options for a wide range of patients.

Your sample will only be used in the future by investigators at Shenzhen Second People's Hospital for scientific research on microorganisms in the lower genital tract and will not be used for commercial purposes or otherwise. The investigator must obtain approval from the Ethics Committee before using your remaining samples in each study.

Specimen preservation and processing: All specimens will be stored in 4℃ refrigerator on the same day after acquisition and DNA will be extracted within 24 hours, DNA specimens will be marked with specimen number and sampling time as required and then freeze stored in -80℃ refrigerator for gynecology department in the central laboratory, and the remaining part will be disposed of in accordance with medical waste disposal process. After the DNA specimens are tested and the results are analyzed, they will be disposed of according to the medical waste disposal process.

3. What you need to do

3.1 Sample collection

In this study, only one additional tube of cervicovaginal secretion will be collected during routine sampling, and the sampling method will be the commonly used clinical sampling method for HPV DNA testing specimens, which will not cause additional collection points and no additional consultation costs. The samples will be collected during routine gynecological examinations and will be divided into one collection, one swab per collection, and one tube in total.

3.2 You will be required to complete 1 study follow-up visit. You will be followed up by telephone 3 months after enrollment. At the follow-up visit, you will be required to cooperate in completing an interrogation survey, where we will ask you about your symptoms related to lower genital tract infections and collect information about your pregnancy.

3.3 Situations in which the study may be terminated.

If the actual samples collected for this project do not meet the testing needs of the project, it may result in the termination of this study and your samples will be destroyed directly. The specific sample requirements for this project are.

(1) Satisfactory nucleic acid extraction of specimens

4. Expected benefits

All subjects participating in the study were exempted from registration fees and routine gynecological examinations (which are necessarily incurred during routine consultations) as financial subsidies for study-related visits and follow-ups.

If we find abnormal results during the testing process, we will inform you by phone.

In addition, research using your identifiable information and identifiable biospecimens may help us understand health and disease, promote improved medical care, promote safer or more effective treatment methods, and expand new scientific knowledge.

5. Expected Cost

There will be no additional cost to you for this study. The registration fee and routine gynecological examinations associated with this study will be waived for you as a financial subsidy, and you will be responsible for the rest of the routine consultation fees.

There is no additional cost to you for this study.

In the event of research-related damage, the sponsor will pay your medical expenses and the corresponding financial compensation in accordance with the laws and regulations.

6. Expected risks

Collection of vaginal and cervical secretions may be slightly uncomfortable and may cause side effects including pain, a little bleeding, and a minimal risk of infection.

Pain: pain can be graded (0-4), ≥1 can be given pain medication

Grading: Grade 0: No pain.

Grade 1 (mild pain): painful but not severe, tolerable, sleep is not affected

Grade 2 (moderate pain): pain is obvious and unbearable, sleep is disturbed, analgesics are requested

Grade 3 (severe pain): severe pain, unbearable sleep severely disturbed, analgesics needed

Bleeding: small amount 0.1-1ml, large amount of bleeding can be stopped by vaginal gauze

Infections.

Mild infection - increased cervical or vaginal discharge, white belt routine indicating cleanliness grade III or leukocytes +++

Moderate - Large amount of discharge with abnormal characteristics, white belt routine indicating cleanliness IV or white blood cells ++++ or BV positive

Severe - with pain or pressure

Treatment options: mild infection - vaginal douching; moderate - vaginal medication based on routine leucorrhea test results; severe - vaginal medication combined with oral anti-infection treatment based on routine leucorrhea test results

*All costs associated with adverse events are borne by the study sponsor and are waived for the subject, including all costs associated with adverse events during and after the trial. In addition, your information may be at risk of privacy breach, but we will do our best to protect your information from unauthorized access by others, including removing information that easily identifies you, and the risk of your identifiable information or identifiable biospecimens being

seen by unauthorized persons is extremely low.

7. Refusal and withdrawal of consent

You have the right to refuse to have the remaining samples stored and refusal to sign this informed consent will not affect any of your rights or interfere with your normal treatment. You may withdraw your consent at any time in the future by contacting your investigator and requesting the immediate destruction of your biospecimen. However, please note that it may not be possible to withdraw if the biospecimen has been anonymized and cannot be traced back to personal information.

8. Privacy Protection

The sample you provide will be coded, i.e., the code number will be used to identify the sample rather than your name or other personal information. Only individual researchers and authorized others will be able to identify you by name from this code. Other researchers conducting future research or you personally will not know which data were generated using your sample.

If the results of the study are clinically relevant, the investigator has an obligation to inform you of this information. At the same time, you should consider the potential consequences and the potential risks to your family and relatives if the information were to be disseminated. For example, if you purchase life insurance or health insurance, you must disclose the results of such studies that may affect your health assessment, a move that could have adverse consequences for you.

The results of future studies involving your sample may be published in medical journals, but we will maintain the confidentiality of your study records as required by law. The personal information of study subjects will be kept strictly confidential and your personal information will not be disclosed except as required by relevant laws. If data is to be transferred to a third party for research use, we will review the qualifications of the third party to ensure the security of the data and sample storage. If necessary, government authorities and hospital ethics committees and other relevant researchers may access your data in accordance with regulations.

9. Transfer of biological samples

In principle, biological samples and related data will be stored in our own or related scientific institutions. If your data must be transferred to a collaborating institution or a third party for research purposes, we will review the qualifications of the collaborating institution or third party and stipulate in the collaboration agreement that the data may only be used for scientific research and not for unauthorized commercial use, and that the use of the data must be strictly in accordance with informed consent, the research protocol and relevant laws and regulations.

10. Feedback on study results

Most studies of biospecimen testing are for research purposes only and do not yet have clear medical implications, so we will not normally give you any feedback on the results of the study. If future studies do reveal results that have implications for your health, the investigator may contact you to inform you of the findings, but this is not required. If the investigator provides you with the results of a genetic test, it may be because the investigator believes you may have a health risk and

recommends that you have the results retested at an accredited clinical testing facility to confirm the results and consult with your physician for the results or with a professional genetic counselor. You are responsible for the cost of these additional follow-up services.

11. Notice of other relevant information

You may ask any questions about this study at any time. Your doctor or researcher will give you his/her phone number so that he/she can answer your questions.

If you have any complaints about participating in the study, please contact the Ethics Office of Shenzhen Second Hospital (contact number: 0755-83464301).

Your doctor will notify you promptly if there is any important new information during the course of the study that may affect your willingness to continue to participate in the study.

If you have questions about the above information, you can ask me. Do you have questions?

Informed Consent Form - Consent Signature Page
Signature Leaflet for Informed Consent

Project name: Clinical study on the analysis of microorganisms in the reproductive tract of infertility based on nucleic acid time-of-flight mass spectrometry

Applicant/research unit: Shenzhen Second People's Hospital

Ethical review approval number: Clinical Research Ethics Committee of Shenzhen Second People's Hospital***

Statement of Consent

I have read the above description of this study and have had the opportunity to discuss and ask questions about this study with my doctor. All of the questions I asked were answered to my satisfaction.

I am aware of the possible risks and benefits of participating in this study. I understand that participation in the study is voluntary, I acknowledge that I have had sufficient time to consider it, and I understand that.

- I can always ask my doctor for more information.
- I can withdraw from this study at any time and will not be discriminated against or retaliated against, and my medical treatment and rights will not be affected.

I am equally aware that if I were to withdraw from this study in the middle of the study, especially if I were to withdraw for medication reasons, it would be very beneficial to myself and the study as a whole if I were to inform my physician of the change in my condition and complete the appropriate physical and physical examinations.

If I need to take any other medication because of my illness, I will seek the doctor's advice beforehand or tell him/her truthfully afterwards.

I give permission for the drug regulatory authority, ethics committee or sponsor's representative to access my study data.

I will be given a signed and dated copy of the informed consent form.

Finally, I decided to agree to participate in this study.

Subject Signature: Date: Month of year Contact no.___

Guardian/authorized delegate Signature: Relationship to subject.

(Note: If the subject is unable to sign informed consent due to incapacity/limited capacity, etc., the subject's guardian or authorized delegate will sign)

Contact Number: Date: Year and Month

I confirm that the details of this study, including their rights and possible benefits and risks, have been explained to the subject and that he or she has been given a copy of the signed informed consent form.

Signature of the researcher: Date: Month and year

Researcher's work telephone number: Mobile phone number

Shenzhen Second People's Hospital Ethics Office Contact Number: 0755-83464301