

Application of WGS-PCR Method in Assisting Identification of *Shigella* spp.

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Abstract

Shigella spp. is the causative agent of shigellosis and one of the category 2 communicable diseases in Taiwan, and it causes an average of 104 local cases per year in recent 5 years. As traditional biochemical tests and serotyping cannot accurately identify some strains of *Shigella* spp., this becomes an obstacle for clinical laboratories to report shigellosis cases to the health departments. To improve the identification of *Shigella* spp., we tested clinical strains of *Shigella* spp. with the whole-genomic-based PCR (WGS-PCR) method. WGS-PCR method allows detection of both the phylogenetic clades of *Shigella* spp. and the *IpaH* gene, an invasive gene plasmid of either *Shigella* spp. or EIEC. Among the 30 confirmed strains of *Shigella* spp., the results of WGS-PCR were 100% concordant with that of serotyping on group B, C and D strains, but only 20% consistency was found on group A strains. While using WGS-PCR to test 29 suspicious strains of *Shigella* spp., 2 group B strains and 2 group D strains were identified, indicating that WGS-PCR may clearly detect suspicious strains. As WGS-PCR method is a low-cost method, we recommend using WGS-PCR as a supplementary test for serotyping.

Keywords: *Shigella*, WGS, PCR

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Update of Negative Pressure Automatic Control System in High Protection Laboratory and Review of Abnormal Events-an Example of Tainan Biosafety Level 3 Laboratory

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Abstract

The outbreak of severe pneumonia with novel pathogens (Covid-19) in 2020 showed the importance of high-protection laboratory (BSL-3/ABSL-3 and above) and biosecurity. We addressed the improvement of the Tainan Biosafety level-3 negative pressure system as an example to demonstrate the functionality and accident handling of a negative pressure laboratory and shared the practical experience for laboratory management in Taiwan. First, each unit was monitored by the negative pressure system according to client's demands. The intake and exhaust fan units were used in main and standby modes in turn. Biological safety cabinet (BSC) exhaust and environmental exhaust were linked to each other. There were three operational modes: the energy save mode, normal mode with BSC low airflow, and normal mode with BSC high air-flow, which saves energy by adjusting the operational situation. All parameters of the laboratory, including the value of negative pressure, temperature, and humidity, were monitored using dynamic graphics and were integrated into the central control system. The administrator could be notified via the network when an abnormal condition occurs. Secondly, according to Article 20, Item 2 of the "Administrative Measures for Infectious Biological Materials", if an abnormal event of negative pressure of high-protective laboratories occurs and cannot be recovered immediately, the event must be reported within 24 hours. Except for immediate recovery, laboratory members should notify the central and local authorities via the laboratory information management system (LIMS) in one day, and then follow the "Regulation of High Protection Laboratory Suspension Procedure" for one month or one-year suspension period. In face of the occurrence of highly infectious diseases internationally, domestic institutions are aware of the urgency

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of disease detection, vaccine development, and the necessary demand for high-protection laboratories. The staff of laboratory biosafety management must keep pace with the times. To maintain normal operations and handle accidental events, the staff should be familiar with basic knowledge and safety principles to avoid biohazards.

Keywords: High protection laboratory, negative pressure automatic control system, abnormal negative pressure, accident notification

week 52, 2022–week1, 2023 (Dec. 25, 2022–Jan. 7, 2023)

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Weekly Data of Notifiable Inases (by week of diagnosis)

| Case diagnosis year | | Week 52★ | | Week 1-52 | | | |
|---------------------------------------|---|----------|---------|--------------|----------------|--------------|----------------|
| Classification | Disease Diagnosed | 2022 | 2021 | 2022 | | 2021 | |
| | | | | Total cases★ | Imported cases | Total cases★ | Imported cases |
| Category I | Plague | 0 | 0 | 0 | 0 | 0 | 0 |
| | Rabies | 0 | 0 | 0 | 0 | 0 | 0 |
| | SARS | 0 | 0 | 0 | 0 | 0 | 0 |
| | Smallpox | 0 | 0 | 0 | 0 | 0 | 0 |
| Category II | Acute Flaccid Paralysis | 5 | 0 | 38 | 0 | 28 | 0 |
| | Acute Viral Hepatitis type A | 3 | 2 | 122 | 2 | 73 | 0 |
| | Amoebiasis | 8 | 3 | 211 | 70 | 192 | 66 |
| | Anthrax | 0 | 0 | 0 | 0 | 0 | 0 |
| | Chikungunya Fever | 0 | 0 | 1 | 1 | 1 | 1 |
| | Cholera | 0 | 0 | 2 | 0 | 0 | 0 |
| | Dengue Fever | 3 | 0 | 85 | 65 | 12 | 12 |
| | Diphtheria | 0 | 0 | 0 | 0 | 0 | 0 |
| | Enterohemorrhagic E. coli Infection | 0 | 0 | 2 | 0 | 0 | 0 |
| | Epidemic Typhus Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Hantavirus syndrome | 0 | 1 | 5 | 0 | 3 | 0 |
| | Malaria | 0 | 0 | 2 | 2 | 2 | 2 |
| | Measles | 0 | 0 | 1 | 0 | 0 | 0 |
| | Meningococcal Meningitis | 0 | 0 | 1 | 0 | 3 | 0 |
| | Paratyphoid Fever | 0 | 0 | 6 | 0 | 2 | 0 |
| | Poliomyelitis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Rubella | 0 | 0 | 0 | 0 | 0 | 0 |
| | Shigellosis | 5 | 1 | 91 | 8 | 123 | 0 |
| Typhoid fever | 1 | 0 | 5 | 3 | 3 | 1 | |
| West Nile Fever | 0 | 0 | 0 | 0 | 0 | 0 | |
| Zika virus infection | 0 | 0 | 0 | 0 | 0 | 0 | |
| Monkeypox | 0 | - | 4 | 4 | - | - | |
| Category III | Acute Viral Hepatitis type B | 1 | 2 | 103 | 0 | 140 | 2 |
| | Acute Viral Hepatitis type C | 16 | 10 | 513 | 1 | 565 | 0 |
| | Acute Viral Hepatitis type D | 0 | 0 | 0 | 0 | 1 | 0 |
| | Acute Viral Hepatitis type E | 0 | 0 | 11 | 0 | 5 | 0 |
| | Congenital Syphilis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Congenital Rubella Syndrome | 0 | 0 | 0 | 0 | 0 | 0 |
| | Enteroviruses Infection with Severe Complications | 0 | 0 | 0 | 0 | 1 | 0 |
| | Haemophilus Influenza type b Infection | 0 | 0 | 2 | 0 | 1 | 0 |
| | Japanese Encephalitis | 0 | 0 | 19 | 0 | 28 | 0 |
| | Legionnaires' Disease | 20 | 3 | 382 | 2 | 360 | 1 |
| | Mumps | 10 | 5 | 306 | 0 | 406 | 2 |
| | Neonatal Tetanus | 0 | 0 | 0 | 0 | 0 | 0 |
| Pertussis | 0 | 0 | 2 | 0 | 0 | 0 | |
| Tetanus | 0 | 0 | 9 | 0 | 5 | 0 | |
| Category IV | Botulism | 0 | 0 | 0 | 0 | 0 | 0 |
| | Brucellosis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Complicated Varicella | 1 | 1 | 35 | 0 | 52 | 0 |
| | Endemic Typhus Fever | 0 | 1 | 17 | 0 | 32 | 0 |
| | Herpesvirus B Infection | 0 | 0 | 0 | 0 | 0 | 0 |
| | Influenza Case with Severe Complications | 1 | 0 | 20 | 1 | 1 | 0 |
| | Invasive Pneumococcal Disease | 8 | 0 | 210 | 0 | 186 | 0 |
| | Leptospirosis | 1 | 1 | 70 | 0 | 82 | 0 |
| | Listeriosis | 4 | 2 | 149 | 0 | 159 | 0 |
| | Lyme Disease | 0 | 0 | 1 | 1 | 1 | 1 |
| | Melioidosis | 0 | 0 | 24 | 1 | 21 | 0 |
| | Q Fever | 0 | 0 | 3 | 0 | 8 | 0 |
| | Scrub Typhus | 3 | 4 | 274 | 0 | 303 | 0 |
| Toxoplasmosis | 0 | 0 | 28 | 0 | 16 | 0 | |
| Tularemia | 0 | 0 | 0 | 0 | 1 | 0 | |
| Category V | Ebola Virus Disease | 0 | 0 | 0 | 0 | 0 | 0 |
| | Lassa Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Marburg Hemorrhagic Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Middle East Respiratory Syndrome | 0 | 0 | 0 | 0 | 0 | 0 |
| | Coronavirus Infections | 0 | 0 | 0 | 0 | 0 | 0 |
| | Novel Influenza A Virus Infections | 0 | 0 | 1 | 0 | 1 | 0 |
| | Rift Valley Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| Severe Pneumonia with Novel Pathogens | 173364 | 154 | 8855669 | 37887 | 16261 | 1714 | |
| Yellow Fever | 0 | 0 | 0 | 0 | 0 | 0 | |

1. ★The weekly and cumulative total numbers include indigenous and imported cases of notifiable infectious diseases.
 2. MDR-TB, Tuberculosis, Syphilis, Gonorrhoea, HIV Infection, AIDS, Hansen's Disease and Creutzfeldt-Jakob Disease are excluded from the table.
 3. Numbers of mumps and tetanus cases are summed up by the week of report.
 4. Since 2022/6/23, " Monkeypox " was listed as a Notifiable Infectious Disease.
 5. Hantavirus Syndrome was applied since September 6, 2021.

Suspected Clusters

- Thirty-two clusters related to diarrhea (20), tuberculosis (4), varicella (1) and upper respiratory tract infection (7) were reported during week 52.

Imported Infectious Diseases

- There were 870 imported cases from at least 19 countries / areas during week 52.
 - Severe Pneumonia with Novel Pathogens:** 863 cases from Japan (37), China (33), Hong Kong (21), Korea (13), Vietnam (6), Thailand (6), Singapore (4), Germany (4), USA (2), Australia (2), the Philippines (2), New Zealand (2), Indonesia (2), Netherlands (1), Macau (1), UK (1), Turkey (1), Malaysia (1), Italy (1), 723 unknowns.
 - Typhoid fever:** 1 case from Thailand (1).
 - Acute Viral Hepatitis type A:** 1 case from Indonesia (1).
 - Dengue Fever:** 3 cases from Indonesia (2), Vietnam (1).
 - Amoebiasis:** 2 cases from Indonesia (2).
- During week 1-52, there were 38048 imported cases from at least 130 countries / areas. The top three countries are Vietnam (4130), USA (2489), Indonesia (1356).
- During week 1-52, the notifiable diseases with the highest number of imported cases is Severe Pneumonia with Novel Pathogens (37887).

Summary of Epidemic

- **Severe Pneumonia with Novel Pathogens :** The new cases of COVID-19 raise in Taiwan, the risk of epidemic spread increase.

Weekly Data of Notifiable Inases (by week of diagnosis)

| Case diagnosis year | | Week 1★ | | Week 1-1 | | | |
|---------------------------------------|---|---------|--------|--------------|----------------|--------------|----------------|
| Classification | Disease Diagnosed | 2023 | 2022 | 2022 | | 2021 | |
| | | | | Total cases★ | Imported cases | Total cases★ | Imported cases |
| Category I | Plague | 0 | 0 | 0 | 0 | 0 | 0 |
| | Rabies | 0 | 0 | 0 | 0 | 0 | 0 |
| | SARS | 0 | 0 | 0 | 0 | 0 | 0 |
| | Smallpox | 0 | 0 | 0 | 0 | 0 | 0 |
| Category II | Acute Flaccid Paralysis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Acute Viral Hepatitis type A | 2 | 3 | 2 | 0 | 3 | 0 |
| | Amoebiasis | 9 | 4 | 9 | 3 | 4 | 0 |
| | Anthrax | 0 | 0 | 0 | 0 | 0 | 0 |
| | Chikungunya Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Cholera | 0 | 0 | 0 | 0 | 0 | 0 |
| | Dengue Fever | 3 | 0 | 3 | 3 | 0 | 0 |
| | Diphtheria | 0 | 0 | 0 | 0 | 0 | 0 |
| | Enterohemorrhagic E. coli Infection | 0 | 0 | 0 | 0 | 0 | 0 |
| | Epidemic Typhus Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Hantavirus syndrome | 0 | 0 | 0 | 0 | 0 | 0 |
| | Malaria | 0 | 0 | 0 | 0 | 0 | 0 |
| | Measles | 0 | 0 | 0 | 0 | 0 | 0 |
| | Meningococcal Meningitis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Paratyphoid Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Poliomyelitis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Rubella | 0 | 0 | 0 | 0 | 0 | 0 |
| | Shigellosis | 1 | 0 | 1 | 1 | 0 | 0 |
| | Typhoid fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | West Nile Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| Zika virus infection | 0 | 0 | 0 | 0 | 0 | 0 | |
| Monkeypox | 0 | 0 | 0 | 0 | 0 | 0 | |
| Category III | Acute Viral Hepatitis type B | 5 | 5 | 5 | 0 | 5 | 0 |
| | Acute Viral Hepatitis type C | 13 | 10 | 13 | 0 | 10 | 0 |
| | Acute Viral Hepatitis type D | 0 | 0 | 0 | 0 | 0 | 0 |
| | Acute Viral Hepatitis type E | 0 | 0 | 0 | 0 | 0 | 0 |
| | Congenital Syphilis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Congenital Rubella Syndrome | 0 | 0 | 0 | 0 | 0 | 0 |
| | Enteroviruses Infection with Severe Complications | 2 | 0 | 2 | 0 | 0 | 0 |
| | Haemophilus Influenza type b Infection | 0 | 0 | 0 | 0 | 0 | 0 |
| | Japanese Encephalitis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Legionnaires' Disease | 11 | 14 | 11 | 0 | 14 | 0 |
| | Mumps | 5 | 4 | 5 | 0 | 4 | 0 |
| | Neonatal Tetanus | 0 | 0 | 0 | 0 | 0 | 0 |
| | Pertussis | 0 | 0 | 0 | 0 | 0 | 0 |
| Tetanus | 0 | 0 | 0 | 0 | 0 | 0 | |
| Category IV | Botulism | 0 | 0 | 0 | 0 | 0 | 0 |
| | Brucellosis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Complicated Varicella | 1 | 0 | 1 | 0 | 0 | 0 |
| | Endemic Typhus Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Herpesvirus B Infection | 0 | 0 | 0 | 0 | 0 | 0 |
| | Influenza Case with Severe Complications | 1 | 0 | 1 | 0 | 0 | 0 |
| | Invasive Pneumococcal Disease | 9 | 2 | 9 | 0 | 2 | 0 |
| | Leptospirosis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Listeriosis | 3 | 1 | 3 | 0 | 1 | 0 |
| | Lyme Disease | 0 | 0 | 0 | 0 | 0 | 0 |
| | Melioidosis | 0 | 0 | 0 | 0 | 0 | 0 |
| | Q Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Scrub Typhus | 2 | 1 | 2 | 0 | 1 | 0 |
| Toxoplasmosis | 0 | 0 | 0 | 0 | 0 | 0 | |
| Tularemia | 0 | 0 | 0 | 0 | 0 | 0 | |
| Category V | Ebola Virus Disease | 0 | 0 | 0 | 0 | 0 | 0 |
| | Lassa Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Marburg Hemorrhagic Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| | Middle East Respiratory Syndrome | 0 | 0 | 0 | 0 | 0 | 0 |
| | Coronavirus Infections | 0 | 0 | 0 | 0 | 0 | 0 |
| | Novel Influenza A Virus Infections | 0 | 0 | 0 | 0 | 0 | 0 |
| | Rift Valley Fever | 0 | 0 | 0 | 0 | 0 | 0 |
| Severe Pneumonia with Novel Pathogens | 182454 | 288 | 182454 | 2314 | 288 | 265 | |
| Yellow Fever | 0 | 0 | 0 | 0 | 0 | 0 | |

1. ★The weekly and cumulative total numbers include indigenous and imported cases of notifiable infectious diseases.
2. MDR-TB, Tuberculosis, Syphilis, Gonorrhea, HIV Infection, AIDS, Hansen's Disease and Creutzfeldt-Jakob Disease are excluded from the table.
3. Numbers of mumps and tetanus cases are summed up by the week of report.
4. Since 2022/6/23, " Monkeypox " was listed as a Notifiable Infectious Disease.
5. Hantavirus Syndrome was applied since September 6, 2021.

Suspected Clusters

- Twenty-four clusters related to diarrhea (15), tuberculosis (2), varicella (1) and upper respiratory tract infection (6) were reported during week 1.

Imported Infectious Diseases

- There were 2321 imported cases from at least 22 countries / areas during week 1.

Severe Pneumonia with Novel Pathogens: 2314 cases from China (580), Japan (53), Korea (16), USA (12), Thailand (10), Vietnam (5), Singapore (5), Hong Kong (4), Malaysia (2), UK (2), New Zealand (2), Australia (2), Turkey (1), Germany (1), Russia (1), Austria (1), Canada (1), France (1), UAE (1), Myanmar (1), and Unknown (1613).

Dengue Fever: 3 cases from the Philippines (1), Indonesia (1), Vietnam (1).

Amoebiasis: 3 cases from Indonesia (3).

Shigellosis: 1 case from Indonesia (1).

Summary of Epidemic

- **Severe Pneumonia with Novel Pathogens :** The new cases of COVID-19 raise in Taiwan, the risk of epidemic spread increase.

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