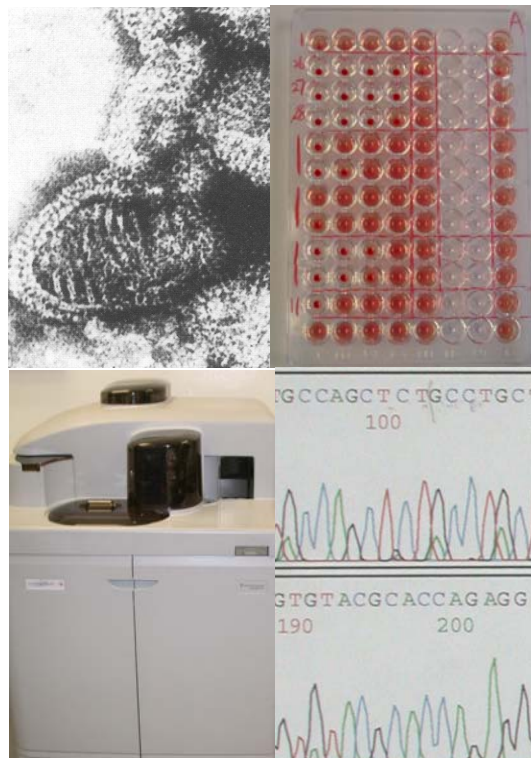


GOVERNMENT VIRUS UNIT

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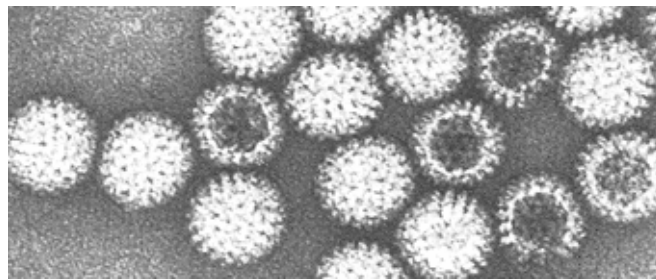
Content

Overview	4
Viral Culture and Serology Laboratory	5
Electron Microscopy Unit	9
Hepatitis Laboratory	10
Human Immunodeficiency Virus Laboratory	11
Molecular Laboratory	12
Cell Culture Laboratory	14
Animal Unit	15
Quality Assurance Activities	16

Overview

The Government Virus Unit is a specialised laboratory for the diagnosis and surveillance of viral, chlamydial and rickettsial infections. It is designated by the World Health Organization as the National Influenza Centre and National Poliovirus Laboratory for the Hong Kong and Macau Special Administrative Regions.

The laboratory processes clinical diagnostic specimens from the public and private sector. Screening for infections and immunity are also performed, such as antenatal screening. The laboratory supports the function of the Department of Health in disease surveillance and outbreak investigation via regular collection of baseline laboratory epidemiological data and timely laboratory diagnostic service. Serological surveys are undertaken to monitor herd immunity. The Unit processes over 250,000 specimens per year.



The Government Virus Unit comprises five major laboratories together with other supportive services located on the 8th to 10th floors of the Public Health Laboratory Centre building, covering a total floor area of approximately 2,500 m². It is designed mainly as a Biosafety Level 2 laboratory, with areas meeting Level 3 requirements for specific operations.

There are five major laboratory testing areas:

- Viral Culture and Serology Laboratory
- Electron Microscopy Unit
- Hepatitis Laboratory
- Human Immunodeficiency Virus Laboratory
- Molecular Laboratory

Two supporting units provide materials and reagents for the above testing activities:

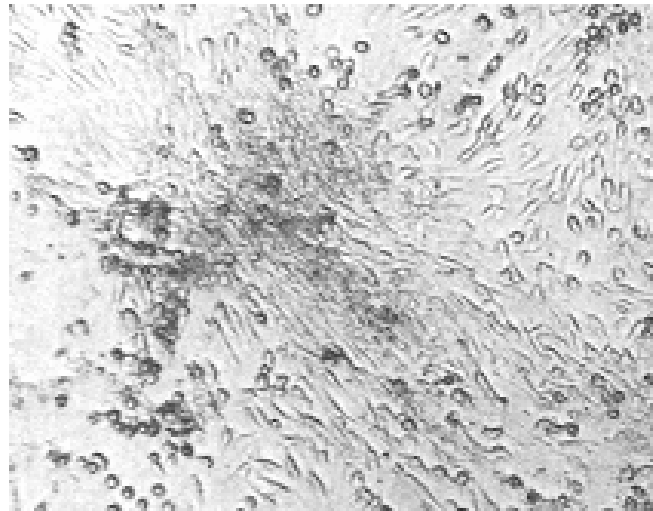
- Cell Culture Laboratory
- Animal Unit

Besides laboratory testing activities, the Unit is actively involved in promoting quality laboratory services in the territory. International, regional and local collaboration is fostered primarily involving monitoring of emergence and re-emergence of various infections, and targeted epidemiological studies on pathogens of public health significance. On-going projects include surveillance on antigenic and genetic changes of influenza virus and poliovirus, and monitoring of molecular epidemiology of human immunodeficiency virus, norovirus and dengue virus.

The Government Virus Unit comprises 3 medical and over 40 scientific and technical staff.

Viral Culture and Serology Laboratory

This laboratory undertakes a range of surveillance and diagnostic activities on various infections. It provides laboratory support in processing specimens obtained from the influenza-like illness, conjunctivitis and gastroenteritis epidemiological surveillance programmes administered by the Department of Health. The laboratory also coordinates the influenza virus and poliovirus surveillance activities within Hong Kong for regular despatch of data to the World Health Organization. Regarding diagnostic testing activities, assays performed include direct antigen detection tests, isolation by cultures, and serological tests for various agents by means of a variety of techniques. Serosurveys for polio, measles, mumps and rubella are undertaken regularly to monitor vaccination programmes. The laboratory covers an area of approximately 200 m².



Tests available in the Viral Culture and Serology Laboratory

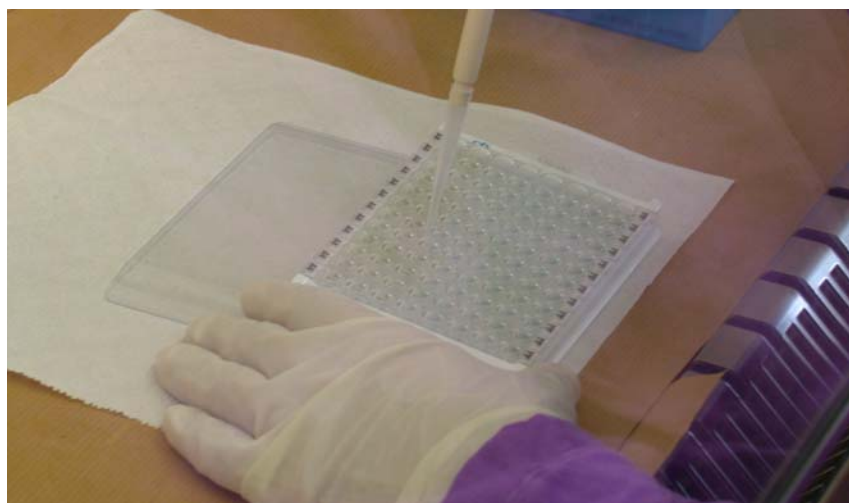
Antigen detection

These comprise mainly immunofluorescence tests performed on aspirates from the respiratory tract to detect various respiratory pathogens, including respiratory syncytial virus, influenza viruses, parainfluenza viruses, and adenoviruses. The Directigen® test for influenza A viruses is also available. Genital, respiratory and conjunctival smears are processed for *Chlamydia trachomatis*, while vesicular lesion smears are tested for herpes simplex and varicella zoster viruses, both using the immunofluorescence technique. Detection of the rabies virus antigen is performed by the immunofluorescence test on various human clinical samples and also on brain tissues of other mammals.



Isolation by culture

A number of cell lines are used routinely for isolation of viruses and *Chlamydia trachomatis*. Shell vial cultures are performed for isolation of cytomegalovirus, measles virus and *Chlamydia trachomatis* respectively in MRC-5, B95a and McCoy cells, followed by definitive identification with the immunofluorescence test. Conventional tube cultures of the following cell lines are inoculated with a range of clinical specimens for virus isolation: HEp-2C, L20B, LLC-MK₂, MDCK, MRC-5, RD and Vero. Identification techniques employed include the immunofluorescence, haemagglutination inhibition and neutralization tests, according to the presumptive virus isolated. Apart from cell cultures, egg inoculation for influenza virus and mice inoculation for rabies virus are also performed.



Serological testing

Agent	Test	Testing methods
Adenovirus	Paired titre	CFT
Chlamydia group	Paired titre	CFT
<i>Coxiella burnetti</i>	Paired titre	CFT
Coxsackie B virus	Paired titre	NT
Cytomegalovirus	Paired titre	CFT
	IgG	CFT; EIA
	IgM	EIA
Dengue virus	Paired titre	HAI
	IgM	IC; EIA
Enterovirus	Paired titre	CFT; NT
Epstein-Barr virus	Paired titre	IFA
	Heterophil IgM	Monospot test
	IgM	IFA
	IgA	IFA
Hantavirus	Paired titre	IFA
Herpes simplex virus	Paired titre	CFT
Influenza A/B virus	Paired titre	CFT; HAI
Japanese encephalitis virus	Paired titre	HAI
<i>Legionella pneumophila</i>	Paired titre	RMAT; IFA
Measles virus	Paired titre	CFT
	IgM	EIA
	IgG	EIA
Mumps virus	Paired titre	CFT
	IgM	EIA
	IgG	EIA
<i>Mycoplasma pneumoniae</i>	Paired titre	CFT; PA
<i>Orientia tsutsugamushi</i>	IgG	EIA
	IgM	EIA
Parainfluenza 1/2/3 virus	Paired titre	CFT
Parvovirus B19	IgG	IFA
	IgM	IFA; EIA
Poliovirus	Paired titre	NT
Rabies virus	IgG	EIA
Respiratory syncytial virus	Paired titre	CFT
<i>Rickettsia conori</i>	Paired titre	IFA
<i>Rickettsia typhi (mooseri)</i>	Paired titre	IFA
Rubella virus	Paired titre	HAI
	IgM	EIA
	IgG	SRH; EIA
<i>Toxoplasma gondii</i>	Paired titre/IgG	IFA
	IgM	IFA
	IgA	IFA
Varicella zoster virus	Paired titre	CFT
	IgG	CFT; EIA

Abbreviations:

CFT - Complement fixation test

EIA - Enzyme immunoassay

HAI - Haemagglutination inhibition test

IC - Immunochromatography

IFA - Immunofluorescence assay

NT - Neutralisation test

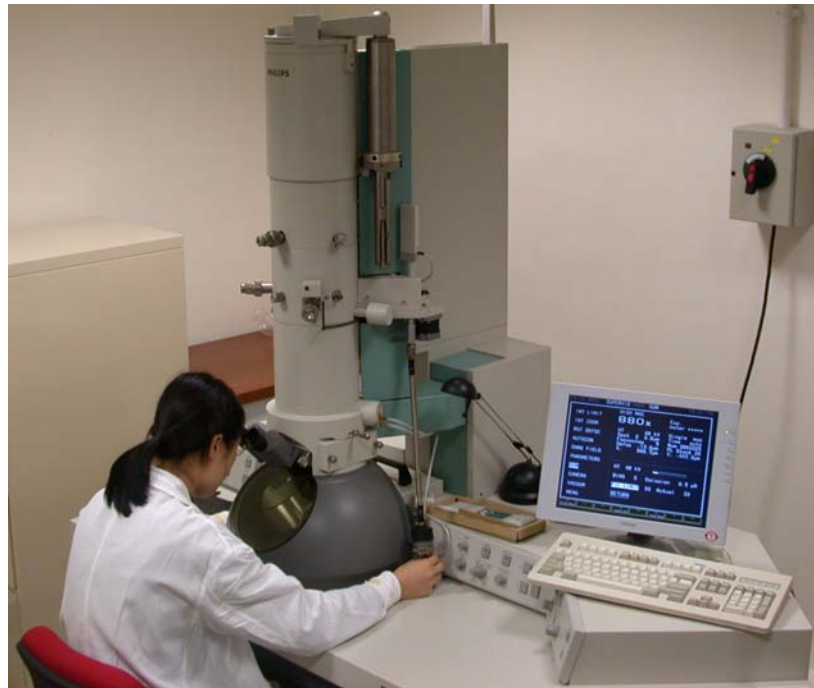
PA - Particle agglutination

RMAT - Rapid microagglutination test

SRH - Single radial haemolysis test

Electron Microscopy Unit

Electron microscopy service is available mainly for detection and identification of viral pathogens directly from clinical specimens. Fluids from cell cultures with atypical changes are also processed for electron microscopy. Specimens, mostly stool samples, are subjected to negative staining before undergoing electron microscopy. The Philips E208S Electron Microscope is currently in service. The laboratory covers an area of approximately 50 m².



Agents detected by Electron Microscopy

Various specimen types are processed in this laboratory. Stool specimens from cases of suspected viral gastroenteritis are received for detection of diarrhoea viruses. Most commonly detected agents include rotaviruses and noroviruses (previously Norwalk-like viruses). Other agents encountered include enteric adenoviruses, astroviruses and sapoviruses (previously Sapporo-like viruses). Vesicular fluid and urine specimens are also received for electron microscopy for detection of viruses in the Herpesviridae family and for polyomaviruses respectively.

Hepatitis Laboratory

Detection of various hepatitis markers is performed for diagnosis of acute infection and immunity screening for hepatitis A to E viruses. Current screening and surveillance programmes include HBsAg testing in the antenatal setting, screening for hepatitis B markers for vaccination purposes, hepatitis B vaccinee follow-up studies, surveillance of drug users for markers of hepatitis B infection, and evaluation of commercial test kits. Immunoassays are employed for the majority of tests. Major equipment in the laboratory include the Architect *i* 2000 analyser, the DIAS system and the Vitros ECi Immunodiagnostic System. The laboratory covers an area of approximately 200 m².



Tests available in the Hepatitis Laboratory

This laboratory processes serum specimens for various markers of hepatitis viruses of clinical significance. Tests performed include:

- Hepatitis A virus: IgM and polyvalent antibodies
- Hepatitis B virus: HBsAg (surface antigen), HBsAb (surface antibody), HBcIgM (core IgM antibody), HBcAb (total core antibodies) and HBeAg/Ab (e antigen/antibodies)
- Hepatitis C virus: IgG antibody
- Hepatitis D virus: Total antibodies
- Hepatitis E virus: IgM and IgG antibodies

Human Immunodeficiency Virus Laboratory

This laboratory offers a range of tests for retrovirus testing. Antibody testing is available for diagnosis of human immunodeficiency virus (HIV) and human T-lymphotropic virus type 1 (HTLV-1) infections. On-going screening and surveillance programmes for HIV include antenatal HIV antibody testing and HIV surveillance in sexually transmitted disease clinic attendees, tuberculosis patients and drug users. Regular unlinked anonymous screening is also carried out for inmates of correctional institutes and methadone clinics. A confirmatory service for presumptive HIV antibody positive cases is offered to other laboratories in the territory. HIV RNA load testing for monitoring drug therapy is performed using a commercial quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) assay. The laboratory covers an area of approximately 200 m².



Tests available in the Human Immunodeficiency Virus Laboratory

A number of tests are available for HIV types 1 and 2 testing. The predominant test is detection of serum antibodies using enzyme immunoassays with the Western blot assay as the supplemental test. Detection of urine antibodies is performed for surveillance among drug users, using the combination of particle agglutination test, enzyme immunoassay and Western blot assay. Plasma viral RNA load is quantified using an RT-PCR assay. Testing for HTLV-1 infection is by means of detection of serum antibodies using the particle agglutination test, supplemented by the Western blot assay.

Molecular Laboratory

This laboratory utilizes molecular techniques for detection of various pathogens in clinical specimens to provide rapid diagnosis, such as detection of noroviruses (previously Norwalk-like viruses) in diarrhoea stool samples. Other tests are performed for guiding clinical management, including the quantitative hepatitis B DNA assay and genotyping of hepatitis C virus. Apart from clinical samples, tests on samples with public health significance are performed, such as viral detection in bivalve shellfish. The molecular epidemiology of various agents is studied with the aid of DNA sequencing. Coupled with phylogenetic analysis, the data could yield useful information for outbreak investigation and epidemiological studies. This laboratory has on-going collaborative projects with institutes in the region on genotyping and epidemiological studies.

Major equipment in this laboratory include thermal cyclers for polymerase chain reaction (PCR), a real-time PCR machine, a gel documentation system and an automated DNA sequencer. The laboratory covers an area of approximately 120 m².



Tests performed in the Molecular Laboratory

Agent	Test	Testing methods
Adenoviruses	Serotyping (cell culture fluid)	PCR; NS
<i>Chlamydia trachomatis</i>	DNA detection and genotyping	PCR; NS
Dengue virus	RNA detection, serotyping and genogrouping	Type-specific RT-PCR; NS
Enteroviruses	Serotyping and genogrouping (cell culture fluid)	RT-PCR; NS
Hepatitis A virus	RNA detection (bivalve shellfish)	Immunocapture RT-PCR; NS
Hepatitis B virus	DNA quantification	Real time PCR
Hepatitis C virus	RNA detection and genotyping	RT-PCR; NS
Hepatitis E virus	RNA detection and genotyping	RT-PCR; NS
Human immunodeficiency virus	Subtyping and resistance testing	RT-PCR; NS
Influenza A virus	H & N subtyping (cell culture fluid)	Subtype-specific RT-PCR; NS
Measles virus	Genotyping	RT-PCR; NS
Norovirus	RNA detection (clinical stool samples)	RT-PCR; NS
	RNA detection (bivalve shellfish)	RT-PCR; NS
Poliovirus	Intratypic differentiation (cell culture fluid)	RT-PCR; NS
Rabies virus	RNA detection	RT-PCR; NS
<i>Rickettsia spp.</i>	DNA detection (ticks)	PCR; NS
Rubella virus	RNA detection	RT-PCR; NS

Abbreviations:

H - Haemagglutinin

N - Neuraminidase

NS - Nucleotide sequencing

PCR - Polymerase chain reaction

RT - Reverse transcription

Cell Culture Laboratory

This laboratory ensures a quality supply of cell cultures in various formats, including conventional tubes, vials and suspensions. Its cell bank houses over 50 cell lines. The cell cultures are used for isolation and identification of viruses and *Chlamydia trachomatis*, and for various serological tests. Quality control measures on cell cultures include assays for sterility, toxicity, mycoplasma detection, and sensitivity in supporting isolation of various agents. In addition, this laboratory assists in maintaining the quality of water supply in the territory by regularly testing water samples from the Water Services Department for the presence of enteroviruses. The methods used include plaque assay, cell culture and polymerase chain reaction. This laboratory covers a floor area of approximately 80 m².



Cell lines routinely maintained in the Cell Culture Laboratory

Cell lines	Usage
B95	Cell smears for immunofluorescence test for Epstein-Barr virus serology
B95a	Measles shell vial culture
HEp-2C	Virus isolation in tube culture
	Neutralization test for adenovirus and enterovirus identification
	Neutralization test for enterovirus serology
L20B	Poliovirus isolation in tube culture
	Neutralization test for poliovirus identification
LLC-MK ₂	Virus isolation in tube culture
McCoy	<i>Chlamydia trachomatis</i> shell vial culture
MDCK	Virus isolation in tube culture
MRC-5	Virus isolation in tube culture
	Cytomegalovirus shell vial culture
RD	Virus isolation in tube culture
	Neutralization test for enterovirus identification
Vero	Virus isolation in tube culture

Animal Unit

This unit keeps a supply of laboratory animals to provide various test reagent components. The unit covers an area of approximately 300 m².

Animals maintained in the Animal Unit

Chickens are kept in the unit to provide red cells for haemagglutination tests for influenza virus identification and for biotyping of *Vibrio cholerae* O1 strains. Geese provide red cells for haemagglutination inhibition tests for rubella virus and flavivirus (dengue and Japanese encephalitis virus) serology. Guinea pigs are the source of red cells for haemadsorption tests for presumptive identification of a number of viruses, especially influenza and parainfluenza viruses. Guinea pig red cells are also used in the haemagglutination and haemagglutination inhibition tests for influenza virus identification and serology assays. In addition, guinea pigs provide complement for use in the complement fixation serology test. Mice are kept in the unit for isolation of rabies virus.

Quality Assurance Activities

The Government Virus Unit strives to provide a quality laboratory service, and is an active participant in various quality assessment programmes on laboratory testing. These include the National External Quality Assessment Scheme of the United Kingdom, the Centers for Disease Control and Prevention of the United States, the National Serology Reference Laboratory of Australia. In addition, the Government Virus Unit avidly promotes quality among local medical laboratories. The Unit collaborates with the Hong Kong Medical Technology Association in the administration of a territory-wide quality assurance programme for diagnostic virology laboratories in Hong Kong. Furthermore, a testing service is provided to ensure the quality of viral vaccine products used in the local immunization programme.