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Communicable Diseases WATCH

衞生防護中心 Centre for Health Protection 衞生署 Department of Health

FEATURE IN FOCUS

Drug-resistant Tuberculosis

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Global picture

Despite the availability of standard tuberculosis (TB) treatment and the advent of rapid diagnostic tools and novel drugs, the global epidemic of tuberculosis (TB) continues alongside the crisis of multidrug-resistant (MDR) TB. In 2015, there were an estimated 10.4 million new TB cases worldwide,[1] including an estimated 480 000 cases of MDR-TB and an additional 100 000 cases of rifampicin-resistant TB (RR-TB). Only 132 120 (23%) RR/MDR-TB cases were notified to the World Health Organization (WHO). India, China and the Russian Federation accounted for 45% of RR/MDR-TB. An estimated 3.9% of new cases and 21% of previously treated cases had MDR/RR-TB. Among MDR-TB cases, an estimated 9.5% had extensively drug-resistant TB (XDR-TB), which was MDR-TB with additional bacillary resistance to any fluoroquinolone and at least one of the second-line injectable agents.

Local drug resistance scene

In Hong Kong, the notification rate of TB decreased from a peak of 697 per 100 000 population in 1952 to 60.1 per 100 000 population in 2016 (provisional figure) (Figure 1).[2] MDR-TB and XDR-TB rates were around 1% (Figure 2) and 0.1% respectively.[2] There is no room for complacency, however, given the substantial drug resistance rates in neighbouring areas and the increasingly frequent population movements. When left untreated, MDR-TB and XDR-TB transmit in the community.[3]

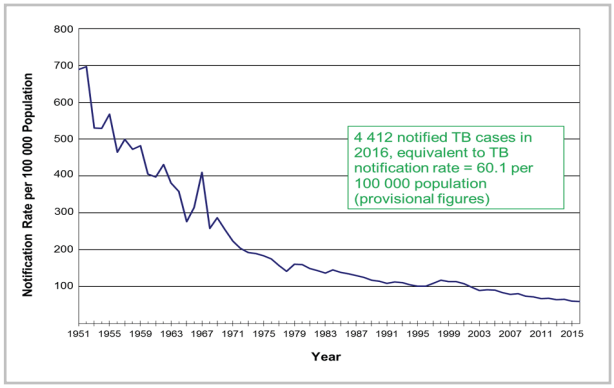

Figure 1 - TB notification rate (all forms) in Hong Kong from 1952 to 2016.

Detection of drug-resistant tuberculosis

Controlling the infection at source remains the cornerstone in TB control. The crisis of MDR-TB highlights the importance of rapid diagnosis that enables timely initiation of effective TB treatment. The past decade witnessed the advent of molecular/genotypic tests that rapidly detect TB and drug resistance. WHO has recommended use of Xpert MTB/RIF (a fully automated, real-time DNA-based polymerase chain reaction assay) for rapid detection of TB and rifampicin resistance,[4] and use of Genotype MTBDRsl (a line probe assay) as the initial test for rapidly detecting resistance to fluoroquinolones and the second-line injectables among patients with RR-TB or MDR-TB.[5] In Hong Kong, genotypic drug susceptibility tests for rifampicin, isoniazid, fluoroquinolone and second-line injectables are increasingly utilised to better inform the initial choice of drugs, pending complementary information from culture-based drug susceptibility testing methods.

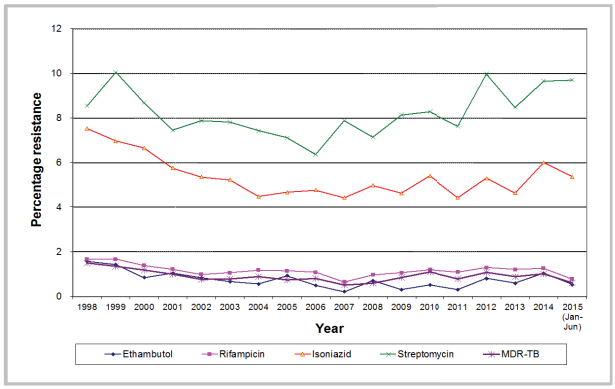

Figure 2 - Trend of anti-TB drug resistance in Hong Kong from 1998 to 2015.

Treatment of drug-resistant tuberculosis

WHO has recently updated treatment guidelines for drug-resistant TB with introduction of a shorter MDR-TB treatment regimen and a new classification for TB drugs (Table 1) that recognises two repurposed agents (linezolid and clofazimine) as core agents and includes two novel drugs (delamanid and bedaquiline) as add-on agents.[6] When bacillary resistance to fluoroquinolones and second-line injectable agents is excluded, or considered highly unlikely, a shorter MDR-TB regimen may be used.[6] The shorter MDR-TB regimen, which comprises four core drugs (moxifloxacin, clofazimine, ethambutol and pyrazinamide) given for nine to 12 months supplemented by three companion drugs (kanamycin, high-dose isoniazid, and ethionamide or prothionamide) in the initial four to six months, is predominantly used among second-line treatment-naïve RR/

MDR-TB patients in settings with a low prevalence of fluoroquinolone-resistant MDR-TB or XDR-TB. When it is inappropriate to give the shorter MDR-TB regimen, WHO recommends a conventional regimen that comprises pyrazinamide and at least four likely effective TB drugs (one chosen from Group A, one from Group B, and at least two from Group C).[6] If the minimum number of effective TB medicines cannot be composed as given above, an agent from Group D2 and other agents from Groups D3 and D1 may be added. Linezolid has become virtually essential in the treatment of fluoroquinolone-resistant MDR-TB and XDR-TB. Prolonged use of linezolid is required for establishing stable cure, but prolonged use was previously hampered by bone marrow suppression and peripheral neuropathy,[7-9] which have substantially reduced with use of better dosing schedules. When there are insufficient companion drugs in the regimen to protect linezolid, delamanid or bedaquiline is added. WHO has published guidelines for use of delamanid and bedaquiline, both of which are potentially cardiotoxic (clinically manifested as prolonged QT).[10-13] By the end of 2015, at least 70 countries have started using bedaquiline and 39 countries have used delamanid. In Hong Kong, a handful of patients have received delamanid with promising results. Bedaquiline will soon be locally available.

Group	Description	Drugs
A	Fluoroquinolones	Lfx, Mfx, Gfx
B	Second-line injectable agents	Km, Amk, Cm
C	Other core agents	Eto or Pto, Cs or Trd, Lzd, Cfz
D1	Add-on agents: first-line drugs	Z, E, H^h
D2	Add-on agents: novel drugs	Bdq, Dlm
D3	Add-on agents: others	PAS, Ipm-Clv, Mpm-Clv, Amx-Clv, Thz

Table 1 - The latest WHO classification of TB drugs for the treatment of RR-TB and MDR-TB. (Abbreviations: Amk, amikacin; Amx-Clv, amoxicillin with clavulanate; Bdq, bedaquiline; Cfz, clofazimine; Cm, capreomycin; Cs, cycloserine; Dlm, delamanid; E, ethambutol; Eto, ethionamide; Gfx, gatifloxacin; H^h, high-dose isoniazid; Ipm-Clv, imipenem-cilastatin with clavulanate; Km, kanamycin; Lfx, levofloxacin; Lzd, linezolid; Mfx, moxifloxacin; Mpm-Clv, meropenem with clavulanate; PAS, para-aminosalicylic acid; Pto, prothionamide; Thz, thiocetazone; Trd, terizidone; Z, pyrazinamide)

Reference

[1]World Health Organization. Global tuberculosis report 2016. WHO/HTM/TB/ 2016.13. WHO Press, WHO, Geneva, Switzerland.

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[10]The use of bedaquiline in the treatment of multidrug-resistant tuberculosis. Interim policy guidance. WHO/HTM/TB/2013.6. WHO, Geneva, Switzerland 2016.

[11]World Health Organization. The use of delamanid in the treatment of multidrug-resistant tuberculosis in children and adolescents: interim policy guidance. WHO/HTM/TB/2016.14. WHO, Geneva 2016.

[12]Tadolini M, Lingtsang RD, Tiberi S et al. First case of extensively drug-resistant tuberculosis treated with both delamanid and bedaquiline. Eur Respir J 2016; 48: 935–938 | DOI: 10.1183/13993003.00637-2016.

[13]Lachâtre M, Rioux C, Dû DL et al. Bedaquiline plus delamanid for XDR tuberculosis. Lancet Infect Dis 2016;16:294.

Update on HIV epidemiology of men who have sex with men in Hong Kong

Reported by Dr Alfred YW SIT, Medical and Health Officer, Dr BY SHU, Senior Medical and Health Officer, and Dr Kenny CHAN, Consultant, Special Preventive Programme, Public Health Services Branch, CHP.

The Department of Health (DH) has implemented a voluntary anonymous case-based HIV and AIDS reporting system with input from both clinicians and laboratories since 1984. The cumulative number of HIV and AIDS reports in Hong Kong reached 8 410 and 1 766 cases as of end 2016.

The annual number of reported HIV infection has continued to increase in the past few years. It reached a record high of 725 cases in 2015, and then showed a mild drop of 4.6% to 692 cases in 2016.

Similar to previous few years, the HIV situation in Hong Kong was still dominated by men who have sex with men (MSM) infections (homosexual and bisexual contact). In 2016, MSM accounted for 61% of all newly reported HIV cases, and 73.7% if excluding cases with undetermined route of transmission due to inadequate information. MSM also accounted for a continually expanding

proportion in the overall male infected cases, from 41.4% in 2006 to 71.1% in 2016 (Figure 1).

The majority of the MSM reported cases in 2016 were Chinese (91%). The median age has been decreasing, from 37 in 2010 to 32 in 2016, which suggested that more younger MSM population was affected. In 2016, the age group of 20 to 29 accounted for the highest proportion among the MSM cases (38.0%), followed by the age group of 30 to 39 (30.7%) (Figure 2).

In 2016, the majority (75.2%) of the reported MSM cases were assessed to have contracted the virus locally, 9.0% in Mainland and 9.9% in other places respectively.

The annual community-based HIV/AIDS Response Indicator Survey (HARiS) continued to be conducted in 2016. Results showed that condom use rates in the last anal sex with emotional relationship partners, regular sex partners and non-regular sex partners were 59.9%, 70.5% and 79.9% respectively. The HIV testing rate within past one year was 58.5%, with another 24.2% never get tested.

Up till now, condom use remains one of the most effective ways to prevent HIV infection. All sexually-active people are advised to practise safer sex by proper and consistent use of condom. As current HIV treatment (highly active antiretroviral therapy (HAART) can effectively control HIV replication, reduce risk of onward HIV transmission, reduce disease progression and improve patients' health, all MSM should test for HIV at least once a year irrespective of their sexual practice. They are also advised to repeat the HIV test after the three-month window period since the last date of unprotected sex. Expanded regular testing of the MSM community would improve early diagnosis, treatment and care for both personal and public health good.

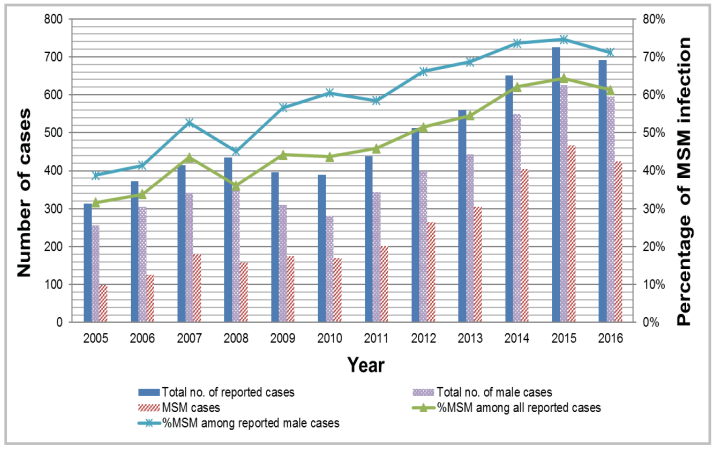
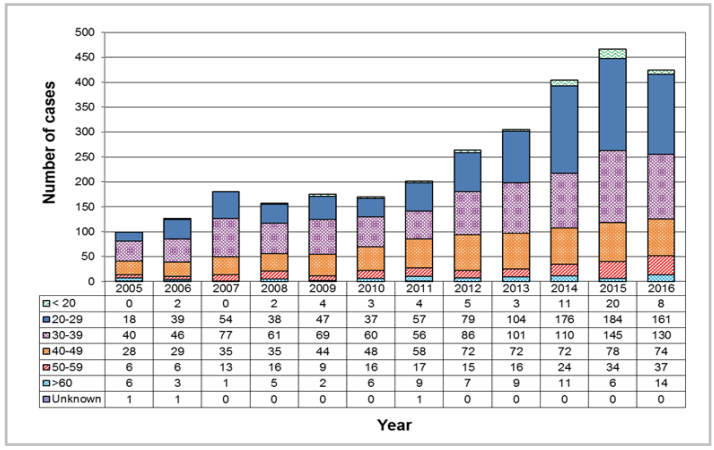


Figure 1 - Proportion of MSM infection among all cases and male cases (2005-2016).



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
< 20	0	2	0	2	4	3	4	5	3	11	20	8
20-29	18	39	54	38	47	37	57	79	104	176	184	161
30-39	40	46	77	61	69	60	56	86	101	110	145	130
40-49	28	29	35	35	44	48	58	72	72	72	78	74
50-59	6	6	13	16	9	16	17	15	16	24	34	37
>60	6	3	1	5	2	6	9	7	9	11	6	14
Unknown	1	1	0	0	0	0	1	0	0	0	0	0

Figure 2 - Age breakdown of HIV-infected MSM cases (2005-2016).

HIV testing services in Hong Kong

People can call DH's AIDS Hotline (2780 2211), Gay Men HIV Testing Hotline (2117 1069) or contact various AIDS non-governmental organisations for free and anonymous HIV testing and counselling services. They may also attend Social Hygiene Clinics (free for eligible person), or consult their family doctors for HIV testing. More information on HIV testing can be found on www.27802211.com and www.21171069.com.

Table 1 - A list of HIV testing services or AIDS Non-governmental Organisations (Services provided may not be limited to MSM).

Department of Health	Website
AIDS Counselling and Testing Service	http://www.info.gov.hk/aids/chinese/hotline/main.htm
Social Hygiene Service	http://www.dh.gov.hk/english/clinictimetable/shc.htm

AIDS Non-governmental Organisations	Phone
A-Backup	3116 7204
AIDS Concern	2394 6677
Project Touch of The Boys' and Girls' Clubs Association	6387 6984
CHOICE	3188 9024
Hong Kong AIDS Foundation	2513 0513
Midnight Blue	2493 4555
Rainbow of Hong Kong	8108 1069
Rainbow Action	6998 1069
The Society of Rehabilitation and Crime Prevention, HK	2323 3983 8206 9922

NEWS IN BRIEF

Workshop on Sterilization and Infection Control related to Operating Theatre on March 1 and 2, 2017

A two-day "Workshop on Sterilization and Infection Control related to Operating Theatre" was conducted on March 1 and 2, 2017, which consisted of a half day visit to the Sterile Supply Department and Endoscopic Reprocessing Unit of Tuen Mun Hospital, together with a 1.5-day didactic lectures. Sessions were ranged from sharing the current practices on equipment validation and packaging requirement, to the future development of sterilisation service. Local and overseas experience on theatre ventilation in preventing infection were also shared. In particular, there was interesting sharing of the new operation theatre design for the upcoming new hospitals in Hong Kong. There were fruitful experiences sharing and exchange, especially on the monitoring, by overseas and local experts through the panel discussion sessions. Audiences were enlightened on the importance of proper sterilisation process and ventilation setup in the operating theatre. All the information has been uploaded onto the Hong Kong Training Portal on Infection Control and Infectious Diseases (http://icidportal.ha.org.hk/).

Photo 1 – Group photo of overseas speakers and workshop organising committee on March 1, 2017.

Photo 2 – Brief introduction on the hospital sterilisation service before hospital visit on March 1, 2017.

Revised classification scheme of countries and areas affected by Zika Virus Infection

A new classification scheme of countries and areas affected by Zika Virus Infection (ZVI) was adopted in the latest Zika virus situation report published by the World Health Organization (WHO) on March 10, 2017. According to the situation report, WHO, the United States Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control have developed a new classification scheme which serves to categorise countries and areas according to the presence of and potential for vector-borne Zika virus transmission. The new scheme classifies countries and areas into four categories instead of three categories adopted in the previous classification. Based on the defined criteria and expert review, some countries and areas were reclassified and some were classified for the first time, bringing the total number of affected countries and areas under the new scheme to 148 (Table 1). The whole situation report can be accessed via the following link: http://www.who.int/emergencies/zika-virus/situation-report/10-march-2017/en/.

Moreover, CDC has recently updated its Zika travel guidance and now recommends that pregnant women should not travel to any area where there is a risk of ZVI, including areas where the virus has been newly introduced or reintroduced and local mosquito-borne transmission is ongoing; areas where the virus was present before 2015 (endemic) and there is no evidence transmission has stopped; and areas where the virus is likely to be circulating but has not been documented. Their recommendation can be found at https://www.cdc.gov/media/releases/2017/s0310-zika-travel-guidance.html.

	WHO Regional Office	Country / territory / subnational area	Total
Category 1: Area with new introduction or re-introduction with ongoing transmission	AFRO	Angola; Cape Verde; Guinea-Bissau	3
	AMRO/PAHO	Anguilla; Antigua and Barbuda; Argentina; Aruba; Bahamas; Barbados; Belize; Bolivia; Bonaire, St Eustatius and Saba; Brazil; British Virgin Islands; Cayman Islands; Colombia; Costa Rica; Cuba; Curacao; Dominica; Dominican Republic; Ecuador; El Salvador; French Guiana; Grenada; Guadeloupe; Guatemala; Guyana; Honduras; Jamaica; Martinique; Mexico; Montserrat; Nicaragua; Panama; Paraguay; Peru; Puerto Rico; Saint Barthelemy; Saint Kitts and Nevis; Saint Lucia; Saint-Martin; St Maarten; St Vincent and the Grenadines; Suriname; Trinidad and Tobago; Turks and Caicos Islands; the United States; the US Virgin Islands; Venezuela	47
	SEARO	Maldives	1
	WPRO	American Samoa; Fiji; Marshall Islands; Micronesia; Palau; Papua New Guinea; Samoa; Singapore; Solomon Islands; Tonga	10
Subtotal			61
Category 2: Area either with evidence of virus circulation before 2015 or area with ongoing transmission that is no longer in the new or re-introduction phase, but where there is no evidence of interruption	AFRO	Burkina Faso; Burundi; Cameroon; Central African Republic; Cote d'Ivoire; Gabon; Nigeria; Senegal; Uganda	9
	AMRO/PAHO	Haiti	1
	SEARO	Indonesia; Thailand; Bangladesh	3
	WPRO	Cambodia; Laos; Malaysia; Philippines; Vietnam	5
Subtotal			18
Category 3: Area with interrupted transmission and with potential for future transmission	AMRO/PAHO	Easter Island (Chile)	1
	WPRO	Cook Islands; French Polynesia; New Caledonia; Vanuatu	4
Subtotal			5
Category 4: Area with established competent vector but no known documented past or current transmission	AFRO	Benin; Botswana; Chad; Comoros; Congo; Democratic Republic of the Congo; Equatorial Guinea; Eritrea; Ethiopia; Gambia; Ghana; Guinea; Kenya; Liberia; Madagascar; Malawi; Mali; Mauritius; Mayotte; Mozambique; Namibia; Niger; Reunion; Rwanda; Sao Tome and Principe; Seychelles; Sierra Leone; South Africa; South Sudan; Togo; Tanzania; Zambia; Zimbabwe	33
	AMRO/PAHO	Uruguay	1
	EMRO	Djibouti; Egypt; Oman; Pakistan; Saudi Arabia; Somalia; Sudan; Yemen	8
	EURO	Georgia; Região Autónoma de Madeira (Portugal); Russia; Turkey	4
	SEARO	Bhutan; India; Myanmar; Nepal; Sri Lanka; Timor-Leste	6
	WPRO	Australia; Brunei Darussalam; China; Christmas Island; Guam; Kiribati; Nauru; Niue; Northern Mariana Islands; Tokelau; Tuvalu; Wallis and Futuna	12
Subtotal			64
Total			148

Table 1 - Classification of countries and areas affected by Zika Virus Infection, published on March 10, 2017.

Locally, the Centre for Health Protection (CHP) of the Department of Health recorded two imported cases of ZVI so far. Our risk assessment and recommendations on the prevention and control of ZVI remained the same. Countries and areas classified under Categories 1 and 2 in WHO's new classification scheme are regarded as those with ongoing Zika virus transmission (affected areas). Pregnant women and women preparing for pregnancy should not travel to affected areas. Moreover, members of the public are reminded to adopt strict anti-mosquito measures and safe sex during travel. Further details of the affected areas can be found at the CHP website (http://www.chp.gov.hk/en/view_content/43209.html).