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THE HONG KONG 香港醫訊
MEDICAL DIARY

VOL.16 NO.4 APRIL 2011



Multidrug-resistant Bacteria



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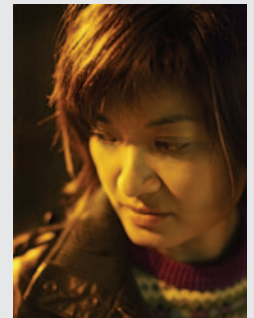
MY FEAST

The photo is part of a large series of wildlife images taken in Tanzania. This vulture is feasting on the carcass of a wildebeest. The stance taken by the vulture is one of being aggressively on guard, protecting its meal.

This photo depicts a predator-prey scenario that is similar to the antibiotic-superbugs war in which humans are increasingly defeated by superbugs as in the carcass.

More of this series of photos will be shown in Dr Amy Pang's talk on "TANZANIA SAFARI" organised in the Combined Scientific Meeting in Anaesthesia, Hong Kong Exhibition & Convention Centre at 15:30 to 17:00, 16 May 2011.

400mm, f8, 1/500sec 19 March 2008



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Published by
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A Losing Battle against Extensively-resistant Bacteria?

Prof. Pak-leung HO

MD, MRCP, FACP, FRCPath, FRCPA, FHKCPath, FHKAM

Editor



Prof. Pak-leung HO

Today, it is difficult to imagine operations or transplantations would be performed without effective antibiotics available for prescription by surgeons as our ancestors did in the pre-antibiotic era. Nonetheless, as antibiotic-resistant superbugs such as the New Delhi Metallo-beta-lactamases (NDM-1), Carbapenemase-resistant *Acinetobacter baumannii* (CRAB), Extensively-Resistant Tuberculosis (XDR-TB) and others hit the headlines, there are increasing concerns that such a situation may be imminent.¹⁻³ Accordingly, the World Health Organization has decided the theme for the year 2011 to be antibiotic resistance. Public awareness campaigns will be launched and WHO will call on governments and stakeholders to implement the policies and practices needed to prevent and to counter the emergence of antibiotic-resistant superbugs. As one of the most densely populated city in the world, Hong Kong is plighted by a multitude of antibiotic-resistant bacteria (Table 1). As bacteria including *Staphylococcus aureus*, *Escherichia coli*, *Acinetobacter baumannii* which are causative agents of the major infectious syndromes - skin and soft tissue infections, pneumonia, urinary tract infections, septicemia - become increasingly resistant to agents that are widely used for their empirical treatment; clinicians face increasing numbers of "hit and miss" situations in the hospital and in the community. While the need for new antibiotics is indisputable, pharmaceutical investment in antibiotic research has declined in the past decade leading to a decreasing number of new antibacterial drugs approved for marketing.⁴ Many large drug companies have announced to exit the antibiotic field completely.⁵ The decisions came as the antibiotic market is perceived to be risky and financially unattractive relative to the chronically administered drugs for treatment of oncological and neurological diseases.⁶

Table 1. The resistance landscape in Hong Kong and potential "hit and missed" situations.

Multidrug resistant	Situation in Hong Kong	Hit-and-missed	Clinical challenges
MDR and XDR-TB	MDR-TB (20 to 40 cases per year), XDR-TB (1-3 cases per year)	Standard short course ineffective	Turnaround time for culture and sensitivity testing often longer than 3 months. Rapid tests not widely accessible to clinicians.
CA-MRSA	Number of cases notified to the Centre for Health Protection was 173 in 2007, 282 in 2008, 368 in 2009 and 495 in 2010.	Resistant to antibiotics widely used to treat skin and soft tissue infections in outpatient settings	Infect patients without healthcare risks
HA-MRSA	6000 to 7000 cases per year in the public hospitals	Resistant to most broad-spectrum antibiotics including the cephalosporins, carbapenems.	Threshold to add anti-MRSA therapy empirically difficult to gauge. Excessive use could lead to emergence of vancomycin resistance.
CRAB	Over 3000 cases found in clinical specimens in 2009	Resistant to almost all beta-lactam antibiotics. Frequent concomitant resistance to fluoroquinolones and aminoglycosides	Only the toxic drug, intravenous colistin was active against >99% of local CRAB
Neisseria gonorrhoeae	Widespread resistance to penicillin, tetracycline and fluoroquinolone		Most patients treated empirically by syndromic approach. Culture often not request.
CRE	Incompletely defined. Sporadic cases (<5 per year) of invasive infections in each major hospital.	No single agent is uniformly active. These bacteria can be resistant to everything, including colistin, fosfomycin and tigecycline.	Klebsiella and E. coli are common causes of many infections.

Multidrug-resistant (MDR) and extensively-resistant (XDR)-tuberculosis (TB); CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*; HA-MRSA, healthcare-associated MRSA; CRAB, Carbapenem-resistant *Acinetobacter baumannii*; CRE, carbapenem-resistant *Enterobacteriaceae*.



This issue visits some of these challenges in the local context. As a profession, we owe to the public our leadership and medical advice on how antibiotics should be used, how emerging antibiotic resistance in the big bugs should be diagnosed, how the spread of resistant bacteria could be slowed down, and how we are tailoring our infection practices in response to stories of successes and failures in its containment elsewhere. There is no simple answer for these challenges. Dr. Thomas Tsang and Dr. TY Wong from the Centre for Health Protection explain for us the Hong Kong Special Administrative Region's public health strategic responses for extensively resistant bacteria. There is no doubt that methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most important antibiotic-resistant bacteria in Hong Kong. In the United States, more patients died because of MRSA infections than of HIV/AIDS and tuberculosis combined. In Hong Kong, the number of patients with MRSA for 2009 was estimated to be about 7000. In the United States, about 7% of all MRSA infections end up fatal. Based on these figures, the 7000 estimation translates to potentially more than 300 and up to 500 MRSA-related deaths in our locality in that year. Even if only 10% of the MRSA infections are preventable, the number of lives saved and unnecessary operations prevented would easily surpass all the benefits associated with preventing all categories of sentinel events combined.⁷ As explained in full by Dr PY Leung, Chief Executive of the Hospital Authority (HA), this is why the authority adopts MRSA infections as a key performance indicator for assessment of patient safety.⁸ In the United Kingdom, since MRSA was taken seriously by the administration in 2005-2006 and a number of measures implemented, the number of MRSA bacteremia across the country has declined drastically from about 7700 per year to less than 2000 per year (Table 2).⁹ As discussed by Dr. Dominic Tsang, the Hospital Authority is committed to benchmark on the successful story from the UK and to introduce evidence-based methods and technologies to better ensure a clean environment for patients.

Table 2. Why the UK succeeded in the war against MRSA?

Key elements of their MRSA control program in the NHS Trust, UK

1. Driven by public reporting of MRSA bacteremia figures
2. Infection control was a clear Trust priority
3. There was strong corporate support and leadership
4. All directorates were involved and had clinical champions
5. There was engagement and support from staff at all levels throughout the Trust

Worldwide, the emergence of Gram-negative bacteria resistant to multiple antibiotics including the carbapenem class is a major threat. In August 2010, the alarming spread of the NDM-1 resistance genes leading to development of carbapenem resistance in *Enterobacteriaceae* has prompted our Centre for Health Protection to set up a territory-wide mechanism for their surveillance. The laboratory detection of carbapenem resistance is not straight-forward. In Hong Kong, a combined phenotypic and genotypic approach is used. The rationale and the protocol are detailed in the article by Dr. Janice YC Lo. In hospital settings, many acinetobacters recovered from clinical specimens have developed resistance to the carbapenem class and multiple other antibiotics. In the tertiary-level hospitals, over 40% of all *Acinetobacter baumannii* isolates are now resistant to the carbapenems. Dr. TC Wu explains the difficulty in treating infections by these carbapenem-

resistant *Acinetobacter baumannii* and details why the existing definition for surveillance requires revision. The local experience confirmed findings reported previously that infections caused by these bacteria were associated with very high mortalities.¹⁰

A decade ago, extended-spectrum beta-lactamase (ESBL)-producing bacteria were almost exclusively found among hospitalised patients, involving mainly *Klebsiella* spp. and the TEM- and SHV- type enzymes. Now, in contrast, the predominant ESBL type is CTX-M and is most commonly detected in *Escherichia coli*. The CTX-M enzymes were most common among isolates associated with urinary tract infections. In the last few years, growing number of CTX-M-producing *E. coli* isolates were identified from patients who are young, healthy and with no history of hospitalisation.¹¹ In Hong Kong, a recent study found that such bacteria were carried by 38% and 27% of household children and adults.¹² The rapid emergence of the CTX-M type ESBL in the community has been attributed to a large reservoir in food animals, carriage by highly mobile genetic elements and dissemination to highly successful lineages of bacteria. The clinical implications of these recent epidemiological developments will be discussed by Dr. Cindy Tse.

Despite Hong Kong's relatively infamous track record in antibiotic resistance, there are stories of success. Thanks to an aggressive programme of tuberculosis control, our incidence of MDR and XDR-TB continues to be low. In the last decade, there is evidence that tuberculous resistance to the first line drugs (ethambutol, streptomycin and isoniazid) is declining. In 2007, community-associated MRSA (CA-MRSA) was made notifiable. Patients with CA-MRSA were screened, treated and given educational advice. Despite an increasing trend, the number of CA-MRSA did not grow exponentially as had been observed in the United States. In 1997, we have the first imported case of vancomycin-resistant enterococcus (VRE). Additional sporadic cases and several small clusters have been found in the subsequent 13 years. Until now, it is not endemic and the total number of cases was very few. As Dr. Vincent Cheng explained, the success is a consequence of several factors – an aggressive approach, single room isolation, and contact screening. For various reasons, almost every cluster of cases was reported in the press. Regarding media reporting, the attitudes and reactions have been mixed. Critics argue that that the reports were sometimes inaccurate, sensational and sometimes demoralising.¹³ Nonetheless, in the UK at least, stories of "dirty hospitals" are evocative, with public acceptance, leading to a cycle of reinforcement that eventually transforms the history of MRSA control in the country.¹⁴ Since 2003, Hong Kong has leaped a big step forward, but "this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning."¹⁵ By all parameters, our war against antibiotic-resistant bacteria is far from winning. The question is - are we serious?

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Carbapenem-resistant or Multidrug-resistant *Acinetobacter Baumannii* - a Clinician's Perspective

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 April 2011.

Introduction

Acinetobacter baumannii has emerged as one of the most troublesome pathogens in the healthcare setting both globally and locally. Its remarkable ability to develop or acquire multiple antibiotic resistance and propensity to survive for prolonged periods under a wide range of environmental conditions, make it a frequent cause of hospital outbreaks and an endemic healthcare associated pathogen. It commonly targets the most vulnerable hospitalised and critically ill patients with breaches in skin integrity who require airway protection, causing pneumonia, urinary tract infection, wound infection and bacteremia.

confirmed by lymph node biopsy and chemotherapy was duly started. However, this was complicated by severe pneumonia resulting in respiratory failure, acute renal failure and septic shock (Figure 1). He was intubated and put on mechanical ventilation in the intensive care unit. Intravenous meropenem was started as empirical therapy with no apparent response. Two days later, his blood and sputum cultures yielded the same carbapenem-resistant *Acinetobacter baumannii* (CRAB) isolate, which was resistant to meropenem and all other tested antibiotics in vitro except amikacin, tigecycline and colistin. After the culture and antibiotic susceptibility profile were reported, the treatment was changed to intravenous colistin. Unfortunately, the patient continued to deteriorate and succumbed 3 days later.

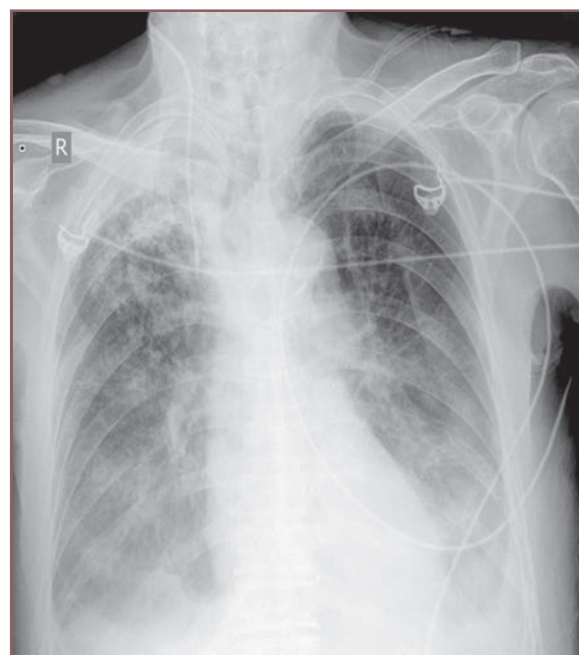


Figure 1. Chest radiograph of a patient with severe CRAB associated pneumonia and bacteremia

An Illustrative Case

A 44 year-old man was admitted to the medical ward for persistent fever and cervical lymphadenopathy. He subsequently developed bilateral pleural effusion and ascites. The diagnosis of Castleman's disease was

Confusion Over Multidrug Resistance

In the literature, various definitions have been used to describe the term multidrug-resistant *A. baumannii* (MDR-AB)¹. Besides causing confusion among clinicians, the diversity of definitions makes it difficult to appreciate how the relative burden of antibiotic resistance in this pathogen differs in different countries. In Hong Kong, the Hospital Authority (HA) currently defines MDR-AB as *A. baumannii* that are concomitantly resistant to all the agents of four antibiotic classes (fluoroquinolones, aminoglycosides, cephalosporins, and beta-lactam/beta-lactamase inhibitor combinations)². Resistance to carbapenems is not considered in the definition. This means an isolate must be resistant to all of the following 13 antibiotics: ciprofloxacin, levofloxacin, gentamicin, netilmicin, amikacin, ceftriaxone, cefotaxime, ceftazidime, cefepime, ampicillin-sulbactam, cefoperazone-sulbactam, ticarcillin-clavulanate and piperacillin-tazobactam, before it is counted as an "MDR-AB". Thus, an isolate resistant to everything except amikacin would not be classified as an MDR-AB by the HA. Likewise, if there is a single "intermediate" susceptibility to any one of the 13 antibiotics, the isolate would also not be regarded as an "MDR-AB". Following through this line of thought, the patient mentioned in the case above will not be reflected to have suffered from an MDR-AB infection in the official statistics as shown in Table 1. Clearly, the operational definition adopted by the HA fails to consider the clinical relevance of the antibiotic

resistance profile and its potential impact on patient outcome. Unsurprisingly, this has previously caused and still continues to cause considerable confusion to clinicians and their subsequent management of affected patients.

Table 1. Multi-drug resistant organisms isolated in the hospitals under the Hospital Authority in 2009

MDRO	Specimen numbers	Numbers of MDROs isolated	MDRO rate
VRE	14,942	28	0.19%
ESBL	103942	20788 to 25985	20% to 25%
CRE	103942	51	0.05%
CRAB	8007	3122	39%
MDRA	8007	320	4%
CRPA	19820	941	4.75%
MRPA	19820	15	0.08%

MDRO, multidrug-resistant organism; VRE, vancomycin-resistant *Enterococcus*; ESBL, extended spectrum beta-lactamase; CRE, carbapenem-resistant *Enterobacteriaceae*; CRAB, carbapenem-resistant *A. baumannii*; MDRA, multi-drug resistant *Acinetobacter*; CRPA, carbapenem-resistant *P. aeruginosa*; MRPA, multi-drug resistant *P. aeruginosa*

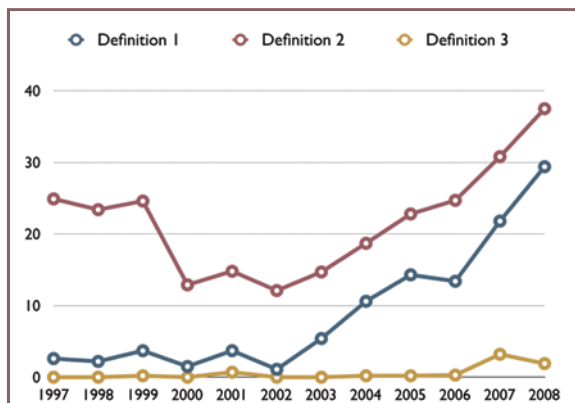


Figure 2. Changes in the multidrug-resistant (MDR) rate according to three different definitions, 1997-2008

Three approaches were used to define MDR-AB³:

1. Resistant to carbapenem class (imipenem and meropenem);
2. Resistance to representative agents from at least three antibiotic classes, including aminoglycosides, antipseudomonal penicillins, carbapenems, cephalosporins and fluoroquinolones;
3. Resistant to all agents or with exception of amikacin

Recently, a study assessed the trends in the resistance profile of *A. baumannii* in Hong Kong over a 12-year period (1997-2008) by using three different definitions and three proxy measures (multidrug resistance rate, cumulative incidence and incidence density) (Figure 2)³. The three definitions were used to represent the two ends and the middle of the spectrum of terminology adopted in the published literature¹. The results showed that observations on secular changes for multidrug resistance in *A. baumannii* ranged from no significant changes to marked increases. It was concluded that the carbapenem class approach performs best³. Firstly, this single antibiotic class approach is currently being used for many established multidrug-resistant bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA), vancomycin-resistant *Enterococci* (VRE) and carbapenem-resistant *Enterobacteriaceae* (CRE). Secondly, the carbapenem class is the drug of choice for serious infections caused by *A. baumannii* infections caused by carbapenem-susceptible strains. Thirdly, CRAB infections are commonly associated with the spread of OXA type carbapenemases, which cause extensive cross resistance to other beta-lactam

antibiotics. Thus, it was suggested that this time-honoured “resistance to a critically important antibiotic class” approach be applied to monitor secular changes in the antibiotic resistance of *A. baumannii*. This approach would also be more relevant and practicable to clinicians.

Epidemiology and Clinical Outcomes of CRAB Infections

For many years, the carbapenem class has been considered as the drug of choice to treat serious *A. baumannii* infections. Until recently, the majority of clinical *A. baumannii* isolates had been sensitive to the carbapenems. As illustrated by the above case, a patient’s culture and sensitivity results are usually not available to guide clinical decision until two to three days later. As a result, critically ill patients are routinely treated with empirical broad-spectrum antibiotics which target the most commonly encountered pathogens. Unsurprisingly, CRAB coverage hence becomes an issue of “hit-and-miss” in these scenarios. In life-threatening infections, broad-spectrum coverage before the infecting organisms are identified is essential because delay in institution of effective therapy within the initial 24 to 48 hours is well recognised to cause poor outcomes⁴⁻⁵. Carbapenems are used in such critical clinical scenarios because it is active against many community- and hospital-acquired pathogens, including extended-spectrum beta-lactamases (ESBL)-producing bacteria. Other advantages include favourable pharmacokinetic and pharmacodynamic properties, good safety profile and extensive clinical experience.

Unfortunately, the rapidly escalating prevalence of CRAB in many parts of the world in the past few years has undermined the reliability of the carbapenem class. To a large extent, the emergence of CRAB was attributed to the horizontal spread of the OXA type of carbapenemase genes (such as OXA-23) to highly successful clones of *A. baumannii*. Besides having resistance to almost all the beta-lactams, these OXA-23 positive bacterial clones are often resistant to the other antibiotics including fluoroquinolones, aminoglycosides and cotrimoxazole⁶⁻⁹. A recent study in Hong Kong reported that the annual CRAB rate has increased from 2.6% in 1997 to 29.4% in 2008. As in other parts of the world, the emergence of CRAB involves clonal spread. Strains with the OXA-23 genes were highly resistant to the carbapenems. In terms of clinical impact, CRAB infections are clearly associated with increases in both the length of hospital stay and mortality particularly in ventilator-associated pneumonia (VAP) and bloodstream infections⁹⁻¹⁰. A study by Sheng WH et al. demonstrated a higher mortality rate in patients with CRAB bacteremia than patients with carbapenem-sensitive *A. baumannii* bacteremia (46% vs. 28.3)¹¹. We have reviewed 34 patients with CRAB infections in a local hospital (Table 2). The crude in-patient hospital mortality rate was 64%. Patients with blood stream infection and pneumonia had the highest mortalities; being 80% and 75%, respectively. While these infections are virtually untreatable, only 5 out of the 34 carbapenem and multidrug-resistant isolates were classified as “MDR-AB” by the HA’s operational definition.



Table 2. Clinical outcomes of carbapenem-resistant *Acinetobacter baumannii* infections by infections sites

Site of Infections	Number of patients	Number of Death (%)
Blood	5	4 (80%)
Chest	16	12 (75%)
Intra-abdomen	8	5 (62.5%)
Wound	3	0 (0%)
Urine	2	1 (50%)
Overall	34	22 (64%)

Treatment of CRAB

At present, the therapeutic options for infections caused by antibiotic-resistant strains of *A. baumannii* are limited (Table 3). Tigecycline is a minocycline derivative with enhanced in-vitro activity against both Gram-positive and Gram-negative bacteria including *A. baumannii*. However, clinical data in treating *A. baumannii* infections remain limited. Breakthrough bacteremia by *A. baumannii* in patients receiving tigecycline has also been reported¹². It is important to note that the emergence of tigecycline resistance may occur while the patient is on treatment¹³. Discrepancy in susceptibility results of tigecycline against *Acinetobacter* spp. due to different methods of testing causes considerable confusion that further hinders its clinical use in *Acinetobacter* infections. Unlike other beta-lactamase inhibitors, sulbactam possesses intrinsic bactericidal activity against *A. baumannii* isolates. Sulbactam containing regimens appear to have equivalent efficacy to other regimens when the isolates are susceptible to sulbactam¹⁴. However, the optimal dosage of sulbactam alone to treat serious *A. baumannii* is unknown.

Limited therapeutic options due to the slow pace of new antibiotic development against highly resistant strains of these pathogens have led to the reconsideration of the therapeutic role of colistin. Colistin, also known as polymyxin E, exerts its antibacterial effect by disturbing the bacterial cell membrane, thus increasing permeability, and eventual cell death. Colistin has retained activity against many multiple drug resistant gram-negative pathogens including *P. aeruginosa* and *A. baumannii*. Though the drug was discovered over 50 years ago, high quality pharmacokinetic data are lacking. Clinical outcomes vary for different types of infections. In general, patients with pneumonia were found to have a low response rate (25%)¹⁵. The poor

performance in pneumonia may be explained by poor penetration into the lung. It was demonstrated that the efficacy of colistin in reducing the bacterial burden was poor in a murine model of pneumonia caused by *A. baumannii*¹⁶. It has been suggested that increased dosage or coadministration of nebulised colistin may increase the response rate. However, higher dosage may increase the risk of side effects such as nephrotoxicity and neurotoxicity. Recently, a randomised controlled study demonstrated no beneficial effects on clinical outcomes of adjunctive nebulised colistin for therapy of Gram negative bacteria associated ventilator-associated pneumonia¹⁷. Renal toxicity is of particular concern in patients with a history of renal impairment, the elderly, and those given concomitant nephrotoxic drugs. However, nephrotoxicity rates are now lower than those previously reported in the 1970s. Dosing should be adjusted in patients with preexisting renal impairment.

Conclusion

A. baumannii is emerging as an opportunistic gram-negative pathogen that targets vulnerable hospitalised patients causes a range of nosocomial infections and that also displays ever-increasing resistance worldwide. Nowadays, it seems that we are losing the antibiotics which can target these highly resistant organisms. Furthermore, the inconsistencies in defining multidrug resistance in this pathogen have caused considerable confusion to both clinicians and researchers. One way to circumvent this is to replace the ill-defined term MDR-AB with CRAB in surveillance programmes. Patients with CRAB infections are clearly associated with high mortality and increased hospital cost which highlights the urgent need for novel strategies in preventing further highly-resistant bacteria emergence, and perhaps a collective approach in facing, addressing and tackling the problem head-on may be the most effective measure in curtailing this threat for the benefit of both our patients and healthcare workers alike.

Table 3. Antibiotics for the treatment of serious *Acinetobacter* infections

Antibiotics	Clinical Efficacy	Tissue distribution	Toxicity	Comments
Intravenous carbapenems (imipenem, meropenem, doripenem)	Excellent	Widely distributed including lung and CNS*	Increase seizure	It cannot be used in CRAB infections
Intravenous tigecycline	Limited clinical data Not recommended in bacteremia	Low serum level achieved due to rapid distribution of tigecycline into tissue and body fluids	Nausea and vomiting	U.S. FDA warning: increased risk of mortality used to treat serious infections, particularly VAP, complicated skin and soft tissue infections and complicated intra-abdominal infections
Intravenous Colistin	Limited clinical data Poor outcomes in pneumonia and bacteremia	Poor lung penetration	Nephrotoxicity & neurotoxicity	Emergence of colistin resistance and associated with colistin use ¹⁸
Intravenous sulbactam	Sulbactam-containing regimens have comparable efficacy to other regimens ¹⁴	Widely distributed except CNS	Well tolerate	Commercially available as combination with ampicillin (unasyn) and cefoperazone (sulperazon) in Hong Kong
Aminoglycosides	Seldom used as monotherapy	Poor lung and CNS penetration	Nephrotoxicity, ototoxicity, neuromuscular blockade	Aminoglycosides and colistin have similar risk of nephrotoxicity ¹⁹

CNS, central nervous system; CRAB, carbapenem-resistant *A. baumannii*; FDA, Food and Drug Administration; VAP, ventilator associated pneumonia



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MCHK CME Programme Self-assessment Questions

Please read the article entitled “Carbapenem-resistant or Multidrug-resistant *Acinetobacter Baumannii* - a Clinician’s Perspective” by Dr. Tak-chiu WU and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 April 2011. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. *Acinetobacter baumannii* has ability to survive for prolonged periods under a wide range of environmental conditions.
2. Hospitalized and critically ill patients are particularly vulnerable to *Acinetobacter baumannii* infections.
3. An *Acinetobacter baumannii* isolate that is concomitantly resistant to ciprofloxacin, levofloxacin, gentamicin, netilmicin, ceftriaxone, cefotaxime, ceftazidime, cefepime, ampicillin-sulbactam, cefoperazone-sulbactam, ticarcillin-clavulanate, piperacillin-tazobactam, meropenem and imipenem but sensitive to Amikacin is classified as multidrug-resistant *Acinetobacter baumannii* (MDR-AB) in the Hospital Authority.
4. Carbapenem-resistant *A. baumannii* (CRAB) isolates often exhibit multidrug resistance involving penicillins, cephalosporins, aminoglycosides and fluoroquinolones.
5. In acinetobacters, carbapenem resistance is associated with the spread of OXA type carbapenemases.
6. CRAB isolates are usually sensitive to piperacillin-tazobactam.
7. In Hong Kong, the incidence rates of CRAB have decreased significantly for the past few years.
8. CRAB infections are commonly associated with high mortality and morbidity.
9. Colistin has retained activity against CRAB but response rate was low in patients with pneumonia because of poor lung penetration.
10. Colistin may cause nephrotoxicity and neurotoxicity.



ANSWER SHEET FOR APRIL 2011

Please return the completed answer sheet to the Federation Secretariat on or before 30 April 2011 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Carbapenem-resistant or Multidrug-resistant Acinetobacter Baumannii - a Clinician's Perspective

Dr. Tak-chiu WU

MRCP, FHKAM(Medicine)
Specialist in Infectious Disease
Associate Consultant, Department of Medicine, Queen Elizabeth Hospital

1 2 3 4 5 6 7 8 9 10

Name (block letters): _____ HKMA No.: _____ CDSHK No.: _____

HKID No.: ____ - ____ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.: _____

Answers to March 2011 Issue

To Optimise Myeloma Treatment in the Era of Targeted Therapy

1. F 2. F 3. F 4. T 5. T 6. T 7. F 8. T 9. T 10. F

Radiology Quiz



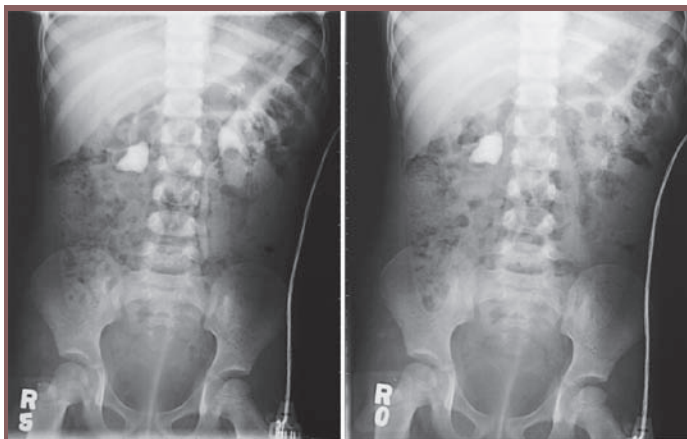
Radiology Quiz

Dr. Wendy LAM

Consultant Radiologist, Department of Radiology,
Queen Mary Hospital



Dr. Wendy LAM



F/4 yrs old
C/O abdominal pain

These are her IVU films taken at 0min and 5min.
1. What are the radiological findings?
2. What is your diagnosis or DDX?

(See P.35 for answers)

The HKSAR's Public Health Response to Extensively Resistant Bacteria

Dr. Andrew TY WONG

MBBS, MSc, FHKAM(Medicine)

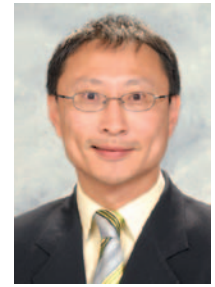
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MBBS, MPH(US), FHKAM(Community Medicine)

Controller, Centre for Health Protection, Department of Health



Dr. Andrew TY WONG

Dr. Thomas HF TSANG

Background

Antimicrobial resistance is an emerging global public health problem¹. The World Health Organization (WHO) and many other health authorities²⁻⁴ are according high priority to the issue. This is clearly reflected by the fact that antimicrobial resistance will be the theme of the coming World Health Day⁵ on April 7, 2011.

The Department of Health (DH) of HKSAR Government is leading a coordinated effort with key partners in addressing the problem of antimicrobial resistance to human health at multiple levels. Under the Centre for Health Protection (CHP), a Working Group named the Health Protection Programme on Antimicrobial Resistance (HPPAR) was formed under the Scientific Committee on Infection Control (SCIC) to give expert advice on prevention and control strategies relevant to local settings. These multi-pronged strategies are described in the following article.

Laboratory Surveillance and Case Reporting

Laboratory surveillance, supported by case reporting from clinicians, provides critical data to measure antimicrobial resistance, monitor its trend, and gauge the effects of interventions. The CHP has been keeping track of various resistant organisms of public health significance through testing of specimens sent by public and private hospitals and outpatient clinics. An Overview of Surveillance of Antimicrobial Resistance by the CHP in Hong Kong⁶ has been published in the *Communicable Diseases Watch* in August 2010 (Table 1). The Public Health Laboratory of CHP provides clinical and/or laboratory advice to frontline clinicians and microbiologists and helps characterisation of bacterial isolates with various resistant phenotypes. A web-based reporting surveillance programme has been established by the Hospital Authority (HA) to standardise surveillance definitions and methodologies and to assess the overall situation of MRSA in public hospitals. Statutory reporting of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections has been in force since January 5, 2007.

Rational Use of Antibiotics

To promote appropriate prescription and rational use of antibiotics by doctors, the CHP, in collaboration

with the Hospital Authority (HA), the University of Hong Kong and The Chinese University of Hong Kong, has developed a handy reference booklet for medical practitioners on the usage of antibiotics. The booklet is named IMPACT (an acronym for Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy) since its first edition published in 1999. The booklet is continuously updated and improved and is now in its 3rd edition (Figure 1)⁷.



Figure 1 - IMPACT 3rd Edition

In hospital settings, antibiotic stewardship programmes have proven to be of great value in monitoring appropriate use of antibiotics. Following a consensus meeting⁸ on "Optimising antimicrobial prescriptions in hospitals by antimicrobial stewardship programme in Hong Kong: rationale and requirement" organised by the SCIC under the CHP in 2005, antibiotic stewardship programmes are now implemented in all HA hospitals.

At the community level, territory-wide publicity campaigns are being conducted to enhance public



knowledge and awareness, making use of television and radio announcements, specially designed posters and pamphlets to promote personal hygiene, hand hygiene and proper use of antibiotics. A special cue card (Figure 2) was developed and given out to patients in HA hospitals and clinics prescribed with antibiotics, offering them important health advice.

While taking antibiotic which is necessary to cure your infection, the antibiotic also kills the normal bacteria in your body and predisposes you to acquire more resistant bacteria.

Therefore, you should enhance personal hygiene by:

1. Practise frequent hand hygiene
2. Eat or drink only thoroughly cooked or boiled items
3. Disinfect and cover all wounds
4. Wear mask if you have respiratory infection symptoms
5. Young children with symptoms of infection should minimize contact with other children

ANTIBIOTIC 抗生素

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使用抗生素可治療細菌感染，但同時亦會殺死身體內之正常細菌，及增加感染抗藥性細菌的風險。

為了保障使用抗生素者的健康，請注意：

1. 時刻保持手部衛生
2. 食水和食物必須徹底煮沸及煮熟
3. 消毒及覆蓋傷口
4. 當有呼吸道感染徵狀時，請戴上口罩
5. 有傳染病徵狀的幼童，應盡可能減少接觸其他兒童

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Figure 2 - Cue card (English & Chinese)

Infection Prevention and Control

Another key strategy is to reduce the emergence and cross-contamination of multi-drug resistant organisms within healthcare settings. To this end, multifaceted control strategies are being implemented, including early case detection and isolation by targeted active screening by cultures of high risk patients, contact precautions, hand hygiene programme, and antibiotic stewardship programme.

In the promotion of hand hygiene, besides regular mass media campaigns, promotional activities have recently been extended to doctors, public hospitals and clinics, private hospitals and long-term care facilities. The Hand Hygiene Awareness Day on May 5, 2010 received broad support and participation from the management and healthcare workers of both public and private health services providers.

Specific programmes have also been designed for the control of multi-drug resistant organisms (MDROs) in residential care homes for the elderly (RCHes), such as the application of infection control bundles and infection control stewardship. The CHP develops and promulgates guidelines on prevention of communicable diseases and infection control, in collaboration with relevant stakeholders, whereas seminars and forums for medical doctors, nurses, infection control practitioners, healthcare workers of long-term care facilities including RCHes and residential care homes for persons

with disabilities (RCHDs), staff working in schools, kindergartens, kindergartens-cum-child care centres and child care centres are organised regularly.

Future Directions

Antimicrobial resistance is going to pose constant challenges globally and locally in the coming years. There are encouraging signs in some areas that control measures are working in Hong Kong, such as a 3.6% reduction in the total number of MRSA cases (from 6,991 cases in 2007 to 6,736 cases in 2009) and over 10% reduction in MRSA infections and bacteremia for acute hospital beds between 2007 and 2009. On the other hand, new threats are presenting themselves, like the emergence of carbapenamase resistant bacteria and multi-drug resistant *Acinetobacter* infections. Hence there is no room for complacency. Recently, HPPAR drew up further enhanced strategies on the control of MDROs and its proposals have been supported by the SCIC. To put them to action as a matter of priority, the Government will coordinate and mobilise partners in public and private medical sectors as well as key players from relevant disciplines, the concerted and collective efforts of which are indispensable in effectively addressing the problem of antimicrobial resistance in Hong Kong.

Table 1. Useful websites on antimicrobial resistance and its control

Internet link
Guidelines developed by CHP on prevention of communicable diseases and infection control, Centre for Health Protection, HKSAR. http://www.chp.gov.hk/en/guideline_infection/346.html
Guidelines for health professionals on antibiotics and relevant health educational materials on proper use of antibiotics for the public, Centre for Health Protection, HKSAR. http://www.chp.gov.hk/en/content/9/460/13039.html
An Overview of Surveillance of Antimicrobial Resistance by CHP in Hong Kong. Communicable Diseases Watch Volume 7, Number 17, Week 32 – 33 (Aug 1 – Aug 14, 2010) http://www.chp.gov.hk/files/pdf/cdw_v7_17.pdf

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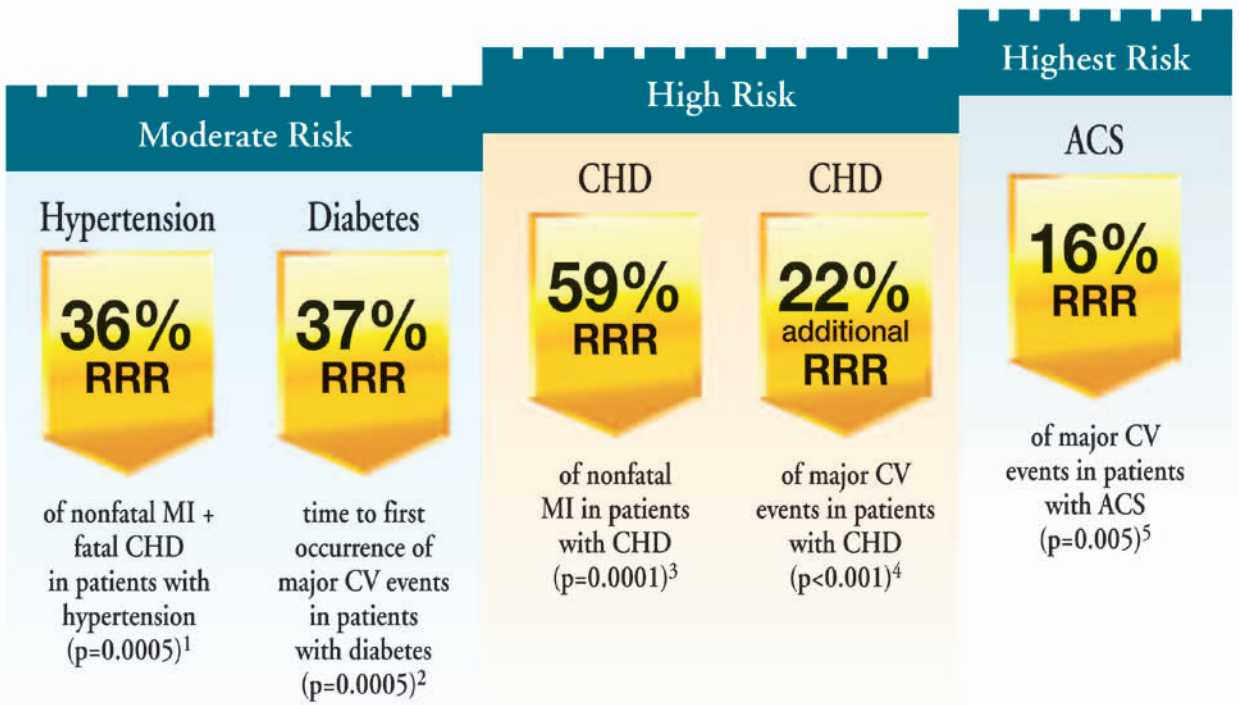
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Making the Control of MRSA a Key Performance Indicator

Dr. PY LEUNG

Chief Executive, Hospital Authority



Dr. PY LEUNG

Health care associated infections have been conceived by many as an intrinsic part of health care. For methicillin-resistant *Staphylococcus aureus* (MRSA), most countries have a prevalence exceeding 25% and the trend is increasing worldwide. In England, for example, the proportion of MRSA bacteremia rose from 2% in 1992 to 44% by 2005. Infections with MRSA have been shown to prolong hospital stay, patient mortality and treatment costs. In Hong Kong, the proportion of MRSA has all along been on the high side, staying at around 40%, and shows no signs of dropping. In 2007, the MRSA bacteremia rate was 0.99 per 1000 patient bed days and 0.19 per 1000 acute patient bed days.

While a much sought after solution for tackling drug resistance is the development of new and effective antimicrobial agents, the investment on research in this area, on the contrary, has been dwindling. The only realistic solution for hospitals, therefore, is to control the spread of MRSA. In the multi-facet approach employed in the UK in 2004, the MRSA bacteremia rate of each National Health Service (NHS) hospital was published and a goal was set to reduce it by 50% by the year 2008.¹ A multidisciplinary working group was set up to implement a comprehensive programme comprising antibiotic stewardship to preserve the efficacy of existing antibiotics, strict adherence of infection control precautions which were packaged as care bundles, targeted screening of high risk patients followed by attempts on eradication, frequent cleaning of 'high touch' areas to reduce environmental contamination and constant emphasis on hand hygiene. Despite limitations such as inadequate supply of single rooms, overcrowding of wards and understaffing in some hospitals, the MRSA bacteremia rate was reduced from 0.47 per 1000 occupied bed days in 2003 to 0.10 in 2008 (Figure 1).¹

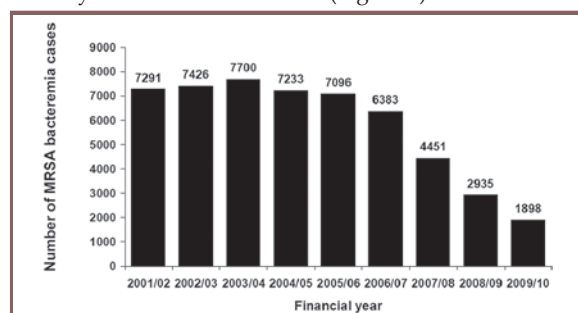


Figure 1. Financial year reports of MRSA bacteremia for acute Trusts in England, 2001-2010.

Note. Figures referred to the number of cases of MRSA bacteremia reported across the NHS.¹

Similar commitment and dedication have been demonstrated in Australia. The rate of MRSA health care associated infections (MRSA HAI) attributed to inpatient care at public hospitals was included as a Key

Performance Indicator (KPI) for the Western Australian Director General of Health since January 2006. In October 2007, surveillance and reporting of MRSA HAI was made mandatory for all public hospitals and private hospitals contracted to provide services for public patients.

What happened in the UK and Australia in the control of MRSA are just examples on the use of an indicator as a tool for hospitals to consistently measure their service performance. Amid concerns on the validity of quality outcome indicators and the generally held belief that infections could not be completely prevented, MRSA bacteremia rate per 1000 acute patient bed days has been chosen as a KPI because it has been shown to carry significant clinical impact. Accurate data collection is readily available through the laboratory information system based on clear definition and protocol. More importantly, the UK experience has aptly demonstrated that with appropriate leadership and resources support, a favourable outcome could be achieved.

Indeed, HA hospitals have responded to the challenge by targeting high risk groups for control, such as patients in the renal units and ICU. To reduce false positive MRSA bacteremia due to contamination in the process of blood taking, which has been shown to mount up to 10%, a well trained phlebotomists team for collection of blood culture is being set up in many hospitals. Additional measures contributing to MRSA reduction include implementation of intravenous catheter care bundle, and the use of rapid molecular method and selective screening agar for case detection. A further boost to MRSA control has also been given by including MRSA bacteremia in the newly launched 'Pay for Performance' (P4P) programme where financial incentives are tied with performance, through self comparison and benchmarking. So far, the results are pretty encouraging, with a more than 10% drop in the HA-wide MRSA bacteremia rate, from 0.19 per 1000 acute patient bed days in 2007 to 0.17 in 2009.

To further reduce MRSA bacteremia, we must adopt it as a sustained priority. Continual search for options in its control is also of paramount importance. Constant improvement of the hospital environment, clinical practice, nursing care, use of antibiotics and bed occupancy would be required. In the end, however, it is the motivation and commitment of our health care teams that drives the performance in reducing MRSA.

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Containment of Antibiotic-resistant Superbugs Through More Robust Cleaning of the Hospital Environment – the Case for Emerging Technologies and Innovations

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Background

In an age when previously sensitive micro-organisms have gradually acquired resistance to multiple antibiotics, hence leading to the emergence of multi-drug resistant organisms (MDRO), nicknamed as “superbugs” by the public media, there have been concerns as to whether affected patients are able to inadvertently spread these MDROs to their non-infected counterparts through the hospital environment, during their stay in the hospital. Thus, there is a recent renewed focus on maintaining an acceptable state of hygiene in the healthcare setting.

Environmental Transmission of MDROs

Thorough cleaning of the hospital environment had never been regarded as crucial in the control of MDROs in the hospital.¹ However, recent studies increasingly showed that contaminated surfaces in hospitals may be a source of transmission of pathogens.² In these studies, patients who were either colonised or infected with nosocomial pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *Clostridium difficile* spores, *Acinetobacter species*, and Norovirus shed these organisms onto their immediate environment. Furthermore, the strains of these drug-resistant micro-organisms in the environment were found to be genotypically identical to those obtained from the very same patients colonised or infected with these organisms.³⁻⁵ Of particular concern is that these pathogens were observed to survive for days, weeks and even up to months (and years for *C. difficile* spores) on various inanimate surfaces, despite requiring no additional growth support.⁶

It is hardly surprising that these organisms are likewise found on a myriad of tactile items in the clinical setting.⁷⁻⁸ For example, all members of the Staphylococcal genus show an avid ability to survive in the environment and on various non-critical items despite wide variations in temperature and humidity, to the extreme even after exposure to sunlight. Furthermore, intermingled with hospital dust, MRSA is still revivable for more than 1 year after inoculation. Following through this line of thought, when healthcare workers touch the contaminated surfaces of MDRO-affected patients' immediate environment without performing adequate hand hygiene afterwards, they will likely transmit this

organism to the next patient they care for, even though the healthcare worker had no direct contact with the affected patient in the first place.⁹⁻¹² This shows that there is an indisputable dynamic relation between MDRO carriers, healthcare workers and their environments regarding pathogen transmission, and it is only natural that this transmission occurs reciprocally.

The Importance of Environmental Decontamination

In view of multiple studies indicating the environment to be an important source of bacterial transmission, more stringent routine environmental decontamination practices in healthcare facilities with regular monitoring is necessary in the MDRO containment bundle. In fact, Hayden et al. showed that reducing environmental contamination through improved cleaning practices of contaminated surfaces significantly reduced VRE acquisition by patients, especially after compliance to a detailed newly introduced cleaning protocol.¹³ Likewise, Gould et al. reported on how environmental cleansing with bleach, environmental samplings, the ready availability and use of hand gel, and admission screening simultaneously implemented in response to an MRSA surge, resulted in a decrease in the number of routine isolations of MRSA. Compellingly, to support the importance of thorough environmental cleansing, the removal of the bleach cleaning process from the containment bundle immediately precipitated a rebound in positive MRSA specimens.

Staff Training

The core elements to successful staff training should include both technical training and education on infection control awareness. Proper staff training on the technical cleansing procedure (Figure 1), with the aid of training videos and standardised cleaning protocols, together with regular monitoring and auditing, and in providing real-time feedbacks on their technical competence to individual staff is essential to help maintain the effectiveness of environmental decontamination. By taking references from the National Health Service (NHS) and Australian standards, implementation of a standardised colour coding scheme to ensure that soiled items should not be used in different areas, enhancing staff compliance to help mitigate the risk of cross-transmission of MDROs.



Figure 1: Staff undergoing training in environmental hygiene in class (photo on the left) and being supervised for technical competence (photo on the right).

The Way Forward

In conjunction with routine environmental deep cleaning methods, in 2009 the National Health NHS has proposed a slew of new technologies that show promises in helping minimise the chance of pathogen-specific recontamination of the environment post-cleaning.¹⁴ These include the use of adenosine triphosphate (ATP) cleaning monitors (Figure 2) to give instantaneous feedback to the cleaning team staff on how effective the cleaning procedure had been carried out, in terms of Relative Light Units (RLU), which is proportional to ATP production and in turn the organic materials or microbial number present. Although it is not a direct assay of MDROs, the measurement of ATP, nonetheless, could serve as a surrogate marker to reflect upon the efficacy of the cleaning procedure on a real-time basis which could not be provided by the conventional bacterial culture method.



Figure 2: ATP measurement by a hand-held device to provide real-time feedback on effectiveness of cleansing.

Recently, a public hospital in Hong Kong has been experimenting with the use of a novel polymer encapsulated chlorine dioxide coupled with zinc chloride disinfectant coating designed by the Hong Kong University of Science and Technology. Once this light chemical is sprayed onto frequently-touched areas of the environment, such as on computer keyboards and mice, it is able to be released and activated immediately upon direct finger contact of the sprayed surface by healthcare workers accessing these equipments, and hence is able to carry out its action in reducing the microbial load of the immediate environment.

Recently, several novel methods to reduce the MDRO burden in the environment have been published (Figure

3). These include routine vacuuming paired with the use of detergent-based cleaning, deep cleaning with disinfectants, and gaseous decontamination with hydrogen peroxide vapour and the use of ultraviolet light room decontamination.¹⁵⁻¹⁹

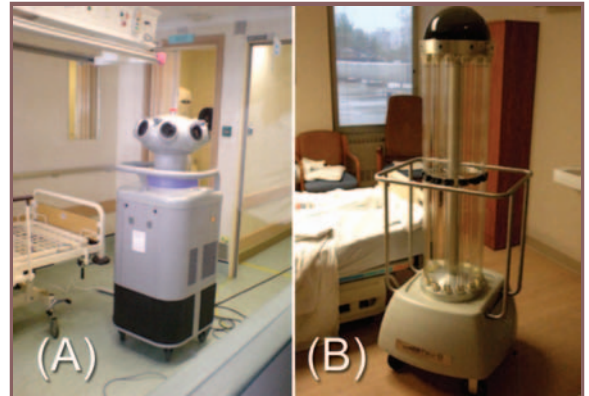


Figure 3A: (A) Equipment set up for gaseous decontamination with hydrogen peroxide vapour in a ward setting. (B) Use of ultraviolet light room decontamination in a patient's room. Courtesy of: Nerandzic et al. BMC Infectious Diseases 2010 10:197.

A 10-month intervention trial that used microcondensation hydrogen peroxide vapour fumigation to decontaminate rooms after they were vacated by patients who suffered from *Clostridium difficile* associated diarrhoea demonstrated that this cleaning technique significantly reduced the incidence of hospital-associated *C difficile* diarrhoea and the MDRO acquisition in patients who were subsequently admitted to the same room. However, despite hydrogen peroxide being effective in destroying micro-organisms and spores, the gas is toxic and frontline staff must take care to completely vacate and seal off all rooms before carrying out the fumigation process, hence this method would best be used after considerable ward movement planning by both the ward and decontamination team in advance, or in the outbreak setting where the MDRO burden would be relatively high, rather than as a routine ward cleaning measure.

A recent study by Nerandzic et al. demonstrated that an automated mobile UV-C light unit, particularly in the 254-nm range was able to reduce bacterial contamination of hospitalised patients' rooms and laboratory bench-top surfaces of *C. difficile*, VRE and MRSA by 2-3 log CFU/cm², 3-4 logs and 2-3 logs respectively. Since this method of decontamination is mobile and relatively easy to manipulate, perhaps it will have a future role to play in a larger-scale environmental decontamination in the hospital setting, particularly in the hope to reduce rates of colonisation or infections with MDROs.

Precisely because it has proven to be difficult for housekeepers to clean and disinfect environmental surfaces consistently despite adhering to hospital guidelines, these new room decontamination technologies come at a very timely fashion and certainly warrant further investigation and on-site trials to determine their cost-effectiveness and their applicability in routine cleaning as well as terminal room disinfection. Thorough cleaning and disinfection of the environment would remain one of the topmost effective preventive measures intended to provide reassurance that patients



as well as staff are not put at unnecessary risks during their stay in the hospital setting and scientific research in this direction would undoubtedly contribute substantially and be awaited with anticipation.

Acknowledgement

The author would like to express his sincerest thanks to Dr Vivien WM Chuang, Ms Doris KW Wong and Dr Naomi HY Cheng for their assistance.

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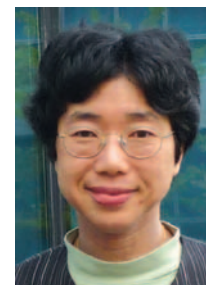
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Laboratory Diagnosis of NDM-1 and Other Carbapenem-Resistant Enterobacteriaceae

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Background

Carbapenems belong to the beta-lactam group of antimicrobials. Compared with earlier beta-lactams, carbapenems have a wide spectrum of anti-bacterial activities and are stable against many types of beta-lactamases produced by bacteria. With the emergence of antimicrobial resistance against multiple agents among bacteria, carbapenems have come to be considered as the last line of defence against resistant infections. As a result, the development of reduced susceptibility of bacteria in the Enterobacteriaceae family to carbapenems, not uncommonly linked to resistance to other antimicrobial classes including fluoroquinolones (such as ciprofloxacin) and aminoglycosides (such as gentamicin and amikacin), heralds the era of untreatable infections.¹

Laboratory Methods for Detection of Antimicrobial Resistance

In the microbiology laboratory, detection of antimicrobial resistance is mainly by means of phenotypic and genotypic methods. Phenotypically, antimicrobial disk diffusion methods and determination of minimum inhibitory concentrations (MICs) are the major techniques employed. In the routine diagnostic laboratory, the disk diffusion method is the most practical choice. Standard guidelines have been promulgated for the performance and quality control of the disk diffusion test, and the most commonly adopted standard in laboratories in Hong Kong is that from the Clinical and Laboratory Standards Institute (CLSI), USA.² Another less commonly used standard locally is that from the European Committee on Antimicrobial Susceptibility Testing (EUCAST).³ The disk diffusion test yields results in categories of "susceptible", "intermediate" and "resistant". Bacterial strains exhibiting the latter two result categories are collectively considered as being "non-susceptible" to an agent. As for MIC determination, results are in terms of mg/L of the antimicrobial agent required to inhibit growth of the strain, and are presented in a continual scale of 2-fold dilutions. MIC determination can be conveniently performed in a routine diagnostic laboratory using commercially available strips impregnated with a gradation of an antimicrobial (such as the Etest), or using automated systems (such as the Vitek system). More conventional standard methods for MIC determination include the broth dilution (micro or macro format) and agar dilution tests. Apart from

the phenotypic methods above, genotypic methods can detect the presence of particular genes conferring resistance to specific antimicrobials. An example is the presence of the NDM gene, encoding for the New Delhi metallo-beta-lactamase, conferring resistance to carbapenems. Genetic testing can also determine the locus and architecture of the resistance mechanism, its transferability and the co-existence of resistance mechanisms of other antimicrobials.

Carbapenemases in Enterobacteriaceae

Although carbapenems are characteristically resistant to hydrolysis by many beta-lactamases, a few groups of enzymes that exhibit carbapenemase activity have been detected among various families of bacteria. An important feature of these enzymes is that they are mostly encoded by mobile genetic elements which may be transferable to other bacterial strains. These enzymes have differential effects on different carbapenems, including imipenem, meropenem, ertapenem and doripenem which are available for clinical use in Hong Kong. Three major classes of carbapenemases of clinical relevance can be detected in members of Enterobacteriaceae (such as *Escherichia coli*, *Klebsiella* spp. and *Enterobacter* spp.).² Class A carbapenemases comprise enzymes such as KPC (K. pneumoniae carbapenemase) and IMI (imipenem-hydrolysing beta-lactamase). Their activity is inhibited by boronic acid in the laboratory. Class B carbapenemases are also called metallo-beta-lactamases (MBLs). Examples include NDM and IMP (active on imipenem). These enzymes can be inhibited by metal-chelating agents such as EDTA in the laboratory. Another group of carbapenemases found in Enterobacteriaceae is the OXA (active on oxacillin) enzymes, mainly OXA-48. They do not have a consistent inhibitor on laboratory testing.

The Status so Far for NDM-1 and Other Acronyms in Hong Kong

NDM was first reported in the literature in late 2009.⁵ In Hong Kong, the Microbiology Division of the Public Health Laboratory Services Branch (PHLSB), Centre for Health Protection (CHP), Department of Health provides diagnostic microbiology and reference laboratory testing services locally to both the public and private sectors. In September 2009, a urinary specimen from a male patient 64 years of age grew an *E. coli* strain with intermediate susceptibility to imipenem. Among

first-line antimicrobials for urinary tract infections, although the strain was resistant by the routine disk diffusion test to ampicillin and amoxicillin-clavulanate, and intermediate to cotrimoxazole, it was susceptible to three other agents (nitrofurantoin, nalidixic acid and levofloxacin). Regarding second line agents, apart from being intermediate to imipenem, the strain was resistant to cephalosporins (cephalexin, cefuroxime, cefoxitin, cefotaxime, ceftazidime and cefepime) and aminoglycosides (gentamicin and amikacin). It was "susceptible" to meropenem and intermediate to ertapenem. The patient recovered after a course of ciprofloxacin. Retrospective testing of the isolate showed that it produced a carbapenemase and harboured the NDM-1 gene.⁶ Since 2009 and up to October 2010, carbapenemase-producing Enterobacteriaceae isolates have been confirmed by the Microbiology Division from 12 patients. There was one patient with an *Enterobacter cloacae* isolate harbouring the Class A carbapenemase IMI-3. For the remaining 11 patients with isolates containing Class B carbapenemases, apart from the NDM-1 strain mentioned above, the remaining 10 patients had strains with the IMP-4 enzyme (two strains of *E. coli*, seven strains of *Klebsiella* spp. and one strain of *Citrobacter freundii*).

Laboratory Surveillance of Enterobacteriaceae Non-susceptible to Carbapenems

In order to monitor the emergence of Enterobacteriaceae with reduced susceptibility to carbapenems, the Microbiology Division has been collating data on such bacterial strains in collaboration with other microbiology laboratories in Hong Kong. Nevertheless, close liaison of the microbiology laboratories with the hospital infection control teams is essential such that isolation precautions for individual patients are adopted immediately on detection of bacterial strains with reduced susceptibility to carbapenems, prior to availability of further characterisation results.

Through discussion among a CHP working group with the participation of clinical microbiologists, clinicians and laboratory scientists, a laboratory protocol has been prepared, recommending testing strategy to screen for Enterobacteriaceae isolates potentially harbouring genes encoding for carbapenemases. As *Proteus* spp., *Providencia* spp. and *Morganella morganii* might exhibit intermediate or frank resistance to imipenem due to non-carbapenemase-mediated mechanisms, these genera were excluded from the enhanced surveillance protocol.⁷ In brief, hospital laboratories were requested to be vigilant for any Enterobacteriaceae strains showing non-susceptibility to any carbapenems. Nevertheless, some bacterial strains producing carbapenemase might still yield "susceptible" results to some carbapenems, such as the NDM-1 strain being susceptible to meropenem as described above. On detection of any Enterobacteriaceae isolate with non-susceptibility to any carbapenem agent using routine susceptibility testing methods, it is recommended to perform the modified Hodge test for carbapenemase production using imipenem, meropenem and ertapenem as substrates.⁷ This test detects the presence of any enzyme that hydrolyses the carbapenem used in

the test (Figure 1a). However, results of this test can be difficult to be interpreted, with occasional indeterminate and false positive/negative findings. For any strain positive or indeterminate in the modified Hodge test, laboratories are requested to perform the combination disk test, essentially routine disk diffusion susceptibility testing with each carbapenem, together with the same carbapenem disk incorporating the inhibitor of Class A carbapenemases (boronic acid) and that of Class B carbapenemases (EDTA) (Figure 1b).⁸ Strains found to possess Class A or B carbapenemase activity should undergo molecular testing for the presence of respective genes by polymerase chain reaction, with confirmation and further characterisation by nucleotide sequencing as necessary.⁹ Clinicians may check with their service laboratories regarding adoption of the protocol as recommended by the working group.

Currently, as there is no readily available screening protocol for Class D carbapenemases, and Enterobacteriaceae strains harbouring this resistance mechanism are not yet globally widespread, systematic surveillance in Hong Kong has not been initiated. Nevertheless, all laboratories should watch out for resistant strains exhibiting carbapenemase activity and being negative for known carbapenemase genes, and subject the isolates for further characterisation as appropriate. Furthermore, as in the case of the NDM gene, new genes mediating resistance will be discovered with time. Any isolate exhibiting uncharacterised resistance mechanisms should be archived for further testing for subsequent newly discovered genes.

Prospect

It is certain that bacteria will continue to evolve, and multi-drug resistance will further emerge. The laboratory plays a crucial role in detecting and monitoring the problem. With changing epidemiological patterns and discovery of new resistance mechanisms, the laboratory needs to be proactive in adopting the most appropriate and up-to-date technology and protocols and surveillance strategies, so as to continue to embrace the challenge against infections by resistant micro-organisms with few therapeutic options.

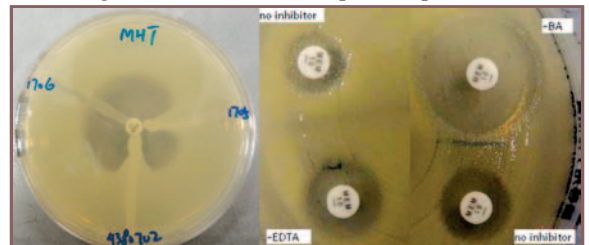


Figure 1. (A). Modified Hodge test demonstrating the production of carbapenemase using the 10 µg meropenem (MEM 10) disk. "1705" was the positive control strain *Klebsiella pneumoniae* ATCC BAA-1705; "1706" was the negative control strain *K. pneumoniae* ATCC BAA-1706; "4380702" was a clinical strain of IMP-4-harbouring *K. pneumoniae* demonstrating carbapenemase production. (B). Combination disk test demonstrating inhibition of carbapenemase activity of the test strain (*Klebsiella pneumoniae* isolate harbouring the KPC-2 enzyme) by boronic acid (BA) (enlargement of inhibition zone diameter of 10 µg meropenem disk by more than 5 mm) and not by EDTA, indicating the presence of a Class A carbapenemase.



Note: The Microbiology Laboratory of the Public Health Laboratory Services Branch, Centre for Health Protection, Department of Health offers clinical microbiology advice and characterisation tests for multi-drug-resistant bacteria. Laboratory surveillance information on multi-antimicrobial resistant bacteria is regularly uploaded to: <http://www.chp.gov.hk/en/epidemiology/29/97/119/564.html>. Contact information of the laboratory can be found on: <http://www.chp.gov.hk/files/pdf/grp-specimenhandbook-en-2004122802.pdf>.

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*Better Healthcare by
Good Management*

Emergence of Extended-spectrum Beta-lactamases in our Community – What does it Mean for Clinicians?

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Dr. Cindy WS TSE

Introduction

Antibacterial resistance in bacteria has been an emerging problem since the discovery of penicillin after World War II. The unnoticed battlefield had been started between the bacteria and humans since the use of antibiotics. The initial penicillin resistance was first detected in *Staphylococcus aureus* after a few years with the use of penicillin. With the introduction of newer β -lactam agents and the discovery of other groups of antibiotics, with the law of natural selection, the bacteria can find the ways and mechanisms to combat the antibiotics we used to kill them. Extended spectrum β -lactamases (ESBL) are only one of them. The third generation cephalosporins were introduced in the 1980s which was an important tool to treat severe infections.⁵ The first report of plasmid-encoded β -lactamases capable of hydrolysing the extended-spectrum cephalosporins was published in 1983. With time goes by, the number of ESBLs is rapidly increasing and the incidences of infections caused by organisms with ESBL have also increased both in the hospital and the community. The worldwide emergence of the multidrug resistant *Escherichia coli* with ESBL in the community has caused difficult selection of the right empirical antibiotics for the community acquired infections.

Types of ESBLs

ESBLs are enzymes that can hydrolyse oximinocephalosporins (cefuroxime, ceftazidime, cefotaxime, ceftriaxone and cefepime) and monobactams (aztreonam) but not cephamycins (cefoxitin and cefotetan) or carbapenem (imipenem, meropenem, doripenem and ertapenem). Most of the ESBLs belong to the Ambler Class A enzyme and they are derived from the parent enzymes of TEM-1, TEM-2 and SHV-1 until 1990s. The picture has changed after the appearance of the CTX-M type ESBL which has emerged and disseminated over the world causing community onset infections especially urinary tract infections. CTX-M enzymes have a high affinity to cefotaxime. The ESBLs are carried on plasmids and are easily transmitted between the gram negative organisms. There are more than 100 types of ESBLs within these families and are detected all over the world. These enzymes can be inhibited by the classical β -lactamase inhibitors which are clavulanic acid, tazobactam and sulbactam.^{4,9}

CTX-M β -lactamases

This group of enzymes are the most prevalent among the non-TEM, non-SHV ESBLs. The name CTX reflects the potent hydrolytic activity of these β -lactamases against cefotaxime. Organisms producing CTX-M-type β -lactamases typically have cefotaxime MICs in the resistant range (64 $\mu\text{g/ml}$), while ceftazidime MICs are usually in the apparently susceptible range. They also hydrolyse cefepime very efficiently. The CTX-M β -lactamases are first isolated in Germany while first reported in nosocomial outbreaks of CTX-M-2 producing *K. pneumoniae*. But from the year 2000, CTX-M producing *E. coli* have become the most important aetiological agents of causing community urinary tract infections and bacteraemia. The emergence of these CTX-M enzymes is referred to as "the CTX-M pandemic".⁸

Risk Factors for the Acquiring Community Onset ESBL Infections

Table 1 summarises risk factors reported to be associated with infections by ESBL-producing bacteria in the community settings.

Table 1 summarises risk factors reported to be associated with infections by ESBL-producing bacteria in the community settings.

Risk factors ^{3, 6-7, 14}	OR
Diabetes ³	4.4
Household contact of a patient with ESBL infection	(16.7% household members are carrier of ESBL organisms)
Previous ESBL+ <i>E. coli</i> colonisation	11.4
Antibiotics within 3 months	15.1
Recent exposure to 3rd G cephalosporins	3.6 - 5.6
Recent exposure to Fluoroquinolones	3.6
Age \geq 65 years	3.5
Male sex	2.9
Travel to endemic areas	India 145.6 Middle East 18.1 Africa 7.7

Laboratory Detection of ESBLs

Most laboratories in Hong Kong are using the Clinical Laboratory Standards Institute (CLSI) guideline when performing the susceptibility testing of the clinical isolates. There are a number of methods recommended for the detection of ESBL in the clinical microbiology laboratory, but most of them are phenotypic tests. Phenotypic tests are more easily done and cost effective. The most commonly used test is the double disk synergy



test (DDST) which is performed on an agar plate with a disk containing cefotaxime (30 µg) and a disk with amoxicillin/clavulanate (20µg/10µg, respectively), placed 30mm apart (centre to centre). Extension of the inhibition zone around the cefotaxime disk indicates the production of ESBL (Figure 1A). Other third generation cephalosporins can also be used for the test.¹⁵

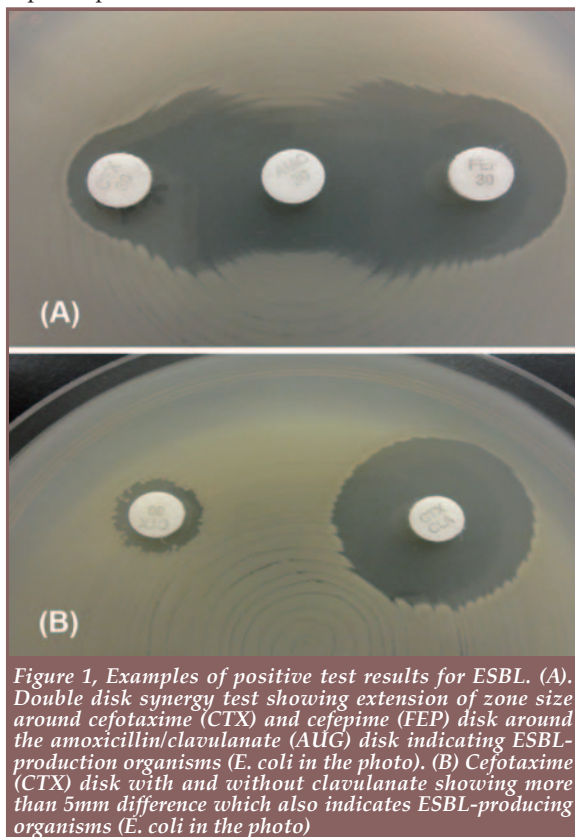


Figure 1, Examples of positive test results for ESBL. (A). Double disk synergy test showing extension of zone size around cefotaxime (CTX) and ceftazidime (FEP) disk around the amoxicillin/clavulanate (AUG) disk indicating ESBL-producing organisms (*E. coli* in the photo). (B) Cefotaxime (CTX) disk with and without clavulanate showing more than 5mm difference which also indicates ESBL-producing organisms (*E. coli* in the photo)

The CLSI recommends disk diffusion test for the clue of ESBL screening for *K. pneumoniae*, *E. coli* and *Proteus mirabilis*. If the zone size of inhibition of ceftazidime, cefotaxime, ceftriaxone, aztreonam or cefodoxime is smaller than the defined zone sizes suggesting of ESBL-producing, the laboratory will need to perform the phenotypic confirmatory test. The CLSI advocates use of cefotaxime (30 µg) or ceftazidime disks (30 µg) with or without clavulanate (10 µg) for phenotypic confirmation of the presence of ESBLs in *K. pneumoniae* and *E. coli*. Disks for use in phenotypic confirmatory tests are available from several suppliers (Becton Dickinson, Oxoid, and MAST). A zone size of ≥ 5 mm difference between the cephalosporin disk with and without clavulanic acid is considered as significant and ESBL producing (Figure 1B). ESBL production can also be detected by commercial methods like E-test or automated system like Phoenix, Vitek 2 and Microscan. However, the specificity is quite variable and depends on whether the laboratory can afford the expensive automatic systems.^{10,15} The tests mentioned above are all phenotypic tests; genetic tests to the molecular level are usually available in reference centres or universities only.

In Hong Kong, ESBL is commonly seen in *Enterobacteriaceae* isolated from clinical specimens. The most common

organisms reported with ESBL positive are the *E. coli* from urinary specimens. Ho et al had conducted studies on antimicrobial resistance in *E. coli* and urine isolates in 2004-2005 and 2006-2008. In the earlier study, 6.6% in 2004 and 10% in 2005 of the *E. coli* from the outpatient urinary specimens were ESBL-producing with CTX-M phenotypes.¹² Another multicentre study on resistance with uropathogens that cause acute uncomplicated cystitis in women in HK showed that 5.2% of the isolates were confirmed to be ESBL-producing and molecular studies showed that they belonged to CTX-M-14, CTX-M-24 and CTX-M-9.¹³

Other ESBL-producing Community Acquired Pathogens

Apart from *E. coli*, *K. pneumoniae* and *P. mirabilis* which can harbour the ESBL enzymes, there were reports showing that these enzymes can also be found in *Salmonella* species, *Shigella sonnei* and *Shigella dysenteriae* which are common cause of bacterial dysentery.¹¹ These will also limit our choice of therapy of treatment as invasive *Salmonella* infections may need parenteral third generation cephalosporins for treatment if they clinically fail to respond to fluoroquinolones which are not uncommonly seen with nalidixic acid resistance.

Clinical Implications of Infections with ESBL-producing Organisms

Why are we so concerned on the infections caused by the ESBL-producing organisms? It is because studies have shown that the empirical and initial treatments with cephalosporins or resistant antimicrobials in patients infected with ESBL-producing *E. coli* or *K. pneumoniae* are usually inadequate and which may lead to a high rate of treatment failures (>80%) and mortality (>35%).¹⁰ One of the important factors determining the outcome of the patients is choosing the right therapy in the early 24-48 hours of presentation. As most of the ESBL-producing *E. coli* and *K. pneumoniae* causing blood stream infections may also be resistant to aminoglycosides, fluoroquinolones and beta-lactam-beta-lactamase inhibitor combinations, choosing the right empirical therapy is not an easy task. The increasing rate of the ESBL-producing organisms causing community acquired infections will force us to use the carbapenem or other potent agents as our empirical therapy for the serious community acquired infections which we do not want to see.

Choice of Antibiotics Therapy

The carbapenems (imipenem, meropenem, ertapenem, doripenem) are still the first choice of treatment for the serious infections with ESBL-producing *E. coli* and *K. pneumoniae*. Studies had showed that >98% of the ESBL-producing *E. coli*, *K. pneumoniae* and *Proteus mirabilis* are still susceptible to these drugs.¹⁰ But with the emergence of the carbapenem-resistant *Enterobacteriaceae*, the "magic bullet" is actually difficult to find.

For uncomplicated urinary tract infections, and



depending on the susceptibility testing of the organisms, agents like amoxicillin/clavulanic acid, fluoroquinolones, nitrofurantoin or cotrimoxazole can also be considered. A recent study showed that the most common organism causing uncomplicated cystitis in women is 77% due to *E. coli*. The antimicrobial susceptibility summary showed that with the 271 isolates of *E. coli*, 92.3% is sensitive to nitrofurantoin, 84.9% of them are sensitive to amoxicillin/clavulanate, 87.1% sensitive to ciprofloxacin and 69.4% sensitive to co-trimoxazole.¹³

There are some older drugs which can be used to treat the ESBL-producing *E. coli* or *K. pneumoniae* infections. Fosfomycin was reported of having excellent in vitro activity against the ESBL-producing *E. coli* or *K. pneumoniae*. In Hong Kong, most of the ESBL-producing *E. coli* isolates were reported to be sensitive to fosfomycin.¹³ Further studies may be needed for the use for other ESBL-producing *Enterobacteriaceae*. Colistin is another choice which we can consider for the treatment of these organisms. Although once considered as quite a toxic antibiotic, it is a last resort that we can consider at the present moment as there is no new anti-gram negative antibiotics available for the treatment of these multidrug resistant organisms. Other than ESBL-producing organisms, actually colistin is used in the treatment of multidrug resistant *Pseudomonas aeruginosa*, carbapenem resistant *Acinetobacter baumannii*. Close monitoring for the development of side effects can improve the safety margin when prescribing the drug. Tigecycline is also one of the drugs in the pipeline which can be considered for treatment.¹⁰

The Way Forward

Bacterial resistance will continue to appear unless we stop using antibiotics which is impossible. The war between bacteria and the human race cannot stop, it's just the time when humans develop the antibiotics or the bacteria develop resistance. The main focus of combating the problem is how we can use the antibiotics wisely and yet not abusing them both in the community and hospital. We hope that there will be new antibiotics against gram negative bacteria soon, but it seems that we do not see the light of finding the new magic bullet yet.

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Table 2, Recommended treatment options for infections with ESBL-producing bacteria

Clinical Conditions	Treatment Options	Remarks
Colonisation	No antibiotics recommended	
Uncomplicated cystitis	Nitrofurantoin, fosfomycin, amoxicillin-clavulanate	
Bacteremia and other invasive infections	Carbapenem class, Piperacillin-tazobactam, amikacin	Amikacin – cannot be used as monotherapy for bacteremia



Why Should Vancomycin-resistant Enterococci (VRE) be under Control in the HKSAR since the First Importation in 1997?

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Introduction

Enterococcus is a facultative anaerobic gram positive coccus which normally colonises our gastrointestinal tract. *Enterococcus faecium* and *Enterococcus faecalis* may cause serious infections, including endocarditis, urinary tract infections, intra-abdominal and pelvic infections, especially in patients with indwelling devices and immunocompromised states. Vancomycin-resistant *E. faecium* and *E. faecalis* (VRE) were first reported in France and the United Kingdom in 1986^{1,2}. Since then, VRE have spread throughout the world and have become an important agent causing nosocomial infections. During the 1990s, a significant increase of VRE was observed in the United States from 0.3% of all isolates in 1989 to over 28% in 2004^{3,4}. Reported risk factors for gastrointestinal colonisation of VRE include hospitalisation, residence in long-term care facilities, use of broad-spectrum antibiotics, renal replacement therapy, and admission to high risk clinical areas⁵⁻⁷. The outbreak of VRE in Europe was mainly related to the widespread use of avoparcin, a vancomycin analogue, in the farm animal industry, while the outbreak in the United States was mostly attributed to the consumption of vancomycin in the healthcare setting⁸. Avoparcin was banned in livestock industry by European Union in 1997, the prevalence of VRE in healthy persons decreased in several European countries⁹. Inappropriate use of vancomycin not only poses a threat to the emergence of VRE, but also vancomycin-resistant *Staphylococcus aureus* (VRSA), involving the in-vivo transfer of vanA genes from VRE to *S. aureus* isolates as has been reported previously¹⁰. As methicillin-resistant *S. aureus* (MRSA) has been endemic in our locality in the past two decades and control of its nosocomial transmission has been difficult, infection control professionals have learnt the importance to combat against the potential outbreaks of VRE and VRSA during the non-endemic phase in Hong Kong.

Epidemiology and Control of VRE in Hong Kong

VRE are uncommon in Hong Kong. Since the importation of VRE in 1997, there have been sporadic cases of VRE colonisation or infections and outbreaks of a limited scale in renal, medicine, and orthopaedic units. In a prospective screening programme of all patients admitted to ten intensive care units between August and November 1999, 2 (0.12%) out of 1697 strains of enterococci were found to be VRE¹¹. In an active surveillance study in a regional hospital between 2001 and 2002, only 1 out of almost 1800 patients being

screened was found to harbour VRE in the stool¹².

Since VRE have not yet disseminated in the community and hospitals in Hong Kong, we are able to focus our resources on the promotion of strategic infection control measures to prevent the nosocomial transmission and outbreak of VRE (Table 1). As enterococci constitute part of the normal gut flora, eradication after their colonisation in the gastrointestinal tract is very difficult and the shedding of VRE can be up to 2 years¹³. Therefore, when there is a sporadic case of VRE being identified in a hospitalised patient, the infection control team will immediately isolate the index case in a single room with strict contact precautions, conduct extensive investigations to find out the source, perform contact tracing of the potential secondary cases, and carry out environmental surveillance and disinfection to control the spread of VRE in our hospitals¹⁴.

Table 1. Infection control measures in prevention of nosocomial transmission of vancomycin-resistant enterococci (VRE) at Queen Mary Hospital

General measures	
1)	Education of infection control practice to healthcare workers
(i)	Mandatory infection control training course for all healthcare workers
(ii)	Collaboration with infection control linked nurses
2)	Enhanced infection control practice
(i)	Enforcement of standard and transmission based precaution in clinical area and provision of alcohol based hand rub in every bed, all ward entrances and corridors
(ii)	Regular environmental cleaning per protocol
3)	Audit of infection control compliance and antibiotic consumption
(i)	Unobtrusive hand hygiene observation and monitoring the consumption of alcohol based hand rub in the hospital
(ii)	Antibiotic stewardship programme to reduce the inappropriate use of vancomycin
Specific measures	
1)	Active surveillance culture for high risk patients
(i)	Patients who had history of hospitalisation or received operation outside Hong Kong in the past 12 months
(ii)	Implementation of rapid diagnostic test to shorten the turn around time and immediately inform Infection Control Team for positive result
2)	Intervention for sporadic case of VRE
(i)	Single room isolation with contact precautions
(ii)	Extensive environmental cleaning sodium hypochlorite 1000 ppm, especially in the toilet
(iii)	"Just-in-time" education session for ward staff
(iv)	Contact tracing for secondary case by VRE screening to all exposed persons in the same ward within a defined period
(v)	Labelling of VRE status at hospital computer system (CMS) and alert Infection Control Team upon patient's readmission

Illustrated Example of an Outbreak Investigation and Control of VRE

On 28 March 2009, VRE was isolated from the catheterised urine in a 77-year-old man (patient 1) hospitalised in the neurosurgical unit of hospital A. The patient was immediately transferred into an isolation room with contact precautions and screening of 28 other patients in the same unit was performed. The VRE

were detected in the stool samples of two other patients including a 62-year-old lady (patient 2) and a 75-year-old man (patient 3). The starting date of the outbreak period was thus defined as 3 March 2009, on which day patient 3 was admitted. Further contact tracing was performed which included 58 patients who had been transferred to the 4 convalescent hospitals since 3 March 2009 and remained hospitalised at the time of investigation. VRE were isolated from the stool of another 89-year-old man (patient 4) who was transferred to hospital B on 16 March 2009. Seventy-one out of 89 patients discharged from hospital A and another 35 patients staying with patient 4 in hospital B were traced and screened for VRE. A total of 192 patients were screened with 3 (1.6%) of them being colonised with VRE. All patients confirmed to be VRE positive were cared for in isolation rooms with contact precautions, and hand hygiene was enforced with an emphasis on directly observed hand hygiene practice. Seven specimens of 7 household members (one specimen each) from patients 1, 2 and 3 were negative for VRE by voluntary screening. A total of 440 and 66 environmental samples were collected in hospital A and hospital B respectively, and two of them taken in hospital B (bedside table and milk container) were positive for VRE.

Our epidemiological investigation showed that patient 4 could be the possible index case of this outbreak. He was directly transferred from a hospital in China and admitted to the neurosurgical intensive care unit for management of chronic subdural haematoma on 3 March 2009, and treated with broad spectrum antibiotics for nosocomial pneumonia. The use of antibiotics may increase the microbial load of VRE and facilitates the nosocomial transmission of VRE to patient 1, 2, and 3. Our case-control study has identified advanced age, presence of indwelling nasogastric tube and endotracheal tube, and the use of beta-lactams antibiotics and vancomycin as the significant risk factors for nosocomial acquisition of VRE. All index and secondary cases were labelled as "VRE carrier" in the hospital information system in order for the infection control team to implement appropriate measures when these patients are re-admitted to the hospital.

Active Surveillance Culture – a Model of "Whom TO Screen"

VRE have recently emerged in Asian countries such as Singapore, Japan, Korea and China¹⁵⁻¹⁸, it has become more difficult to maintain Hong Kong free of VRE. In addition to the ongoing antibiotic stewardship programme to minimise the antibiotic selection pressure¹⁹, we are the first hospital cluster to introduce the active surveillance culture programme to detect the presence of multiple drug resistant organisms among the high risk patients upon admission since December 2009. Basically, it is a model of "whom TO screen". T means "travel" as in medical tourists and O stands for "operation outside Hong Kong". Triage personnel in the emergency room or admission ward will enquire on whether the patient had a history of medical tourism or operation outside Hong Kong in the past 12 months (Figure 1). For patients fulfilling the criteria of TO, the infection control team will follow them up by collecting relevant clinical specimens and coordinate with the laboratory for rapid identification of a panel of resistant

pathogens including MRSA, community-acquired-MRSA, VRE, and the recently identified carbapenem-resistant Enterobacteriaceae (CRE) carrying NDM-1²⁰. Once the colonisation or infection status of multiple drug resistant organisms is confirmed, appropriate infection control practices will be implemented.

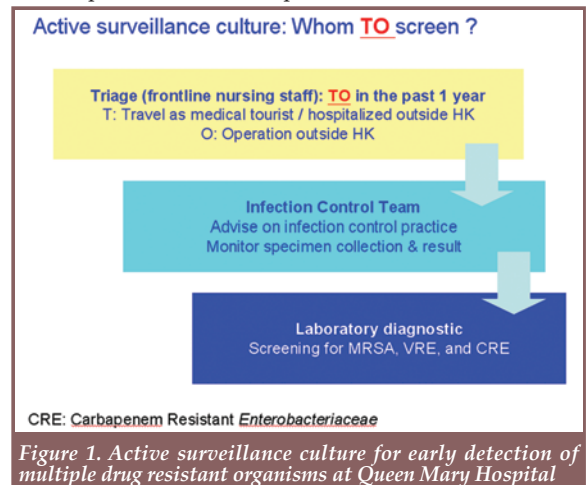


Figure 1. Active surveillance culture for early detection of multiple drug resistant organisms at Queen Mary Hospital

Acknowledgment

We thank our frontline healthcare workers for their active participation in the infection control measures to prevent the nosocomial transmission of multiple drug resistant organisms. The description of the VRE outbreak has been published and permission to reproduce the portion of published material has been obtained from the editorial office of Emerging Health Threats Journal.


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British Medical Association (HK Branch)





Basic Facts on Radiation and Radiation Protection

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Dr. Wah-shan NG

What is Radiation? ^{1, 2, 3, 4, 5, 6}

Radiation is the process when energy is released from a source and travels to a receiving body. It may be in the form of electromagnetic waves (e.g. gamma ray, X-ray, microwave, visible light) or high speed subatomic particles (e.g. alpha-, beta-particles). Radiation can be divided into ionising and non-ionising radiation. Ionising radiation is radiation with sufficiently high energy that can ionise atoms. Most often, this occurs when an electron is stripped from an electron shell, leaving the atom with a net positive charge.

What are the Types of Ionising Radiation?

Alpha α particles have a very short range (a few centimetres in air) but high energy transfer. Our intact skin is an effective barrier against penetration. Hazard will result only if a person has been internally contaminated such as by ingestion or inhalation. **Beta** β particles are moderately penetrating and can go as deep as a few millimetres of body tissue. **Gamma** γ radiation is electromagnetic energy. It is very penetrating and layers of lead are needed for shielding. **Neutron** radiation is the emission of neutrons from the nuclei of radionuclides. It can be very penetrating and requires thick layers of concrete, water or paraffin for shielding. **X-ray** and **positrons** (positively charged electrons) are ionising radiation which are very rarely considered as a concern in nuclear and radiation incidents.

How is it Measure?

The activity of the source of radioactivity is measure in becquerel (Bq) which means one disintegration per second. The old unit is curie Ci ($1 \text{ Ci} = 3.7 \times 10^{10} \text{ Bq}$). The energy deposited per gram in a medium by the radiation, which is the absorbed dose, is measured in Gray (G, $1 \text{ Gy} = 1 \text{ J/Kg}$). Gray can be used for any radiation, but does not represent the biological effect. The biological effect is measured in sievert (Sv), the dose equivalent, and is calculated as the absorbed dose multiplied by the quality factor Q ($S_i = \text{Gy} \times Q$). Q characterised the damaging effects of each type of radiation, which is 1 for X-ray, gamma ray and electrons. We are constantly exposed to background radiation [about 2 millisieverts (mSv) per year in Hong Kong]. For comparison, the radiation dose of a chest radiograph is about 0.06 mSv, flight at high altitude is about 0.005 mSv/Hr.^{1, 4, 5, 6, 7}

Approximate effective radiation dose of common radiological examinations in mSv: CT abdomen 15, CT thorax 7, IVU 3, CT brain 2, Spine X-ray 1.5, mammography 0.4, Chest 0.06, intraoral dental 0.005, extremity 0.001.⁸

How can we Detect Radiation?

Ionising radiation per se is invisible, tasteless and bears no smell. We can detect the existence of ionising radiation by a Geiger-Muller (GM) counter or ionisation chamber.

What are the Biological Effects of Ionising Radiation?

There are two types of biological effects of ionising radiation, namely the Deterministic effects and the Stochastic effects. Deterministic effects are the predictable one when the absorbed dose is more than a threshold level such as nonmalignant skin damage, cataract, haematological effects, acute radiation syndrome (ARS) and impairment of fertility. For the Stochastic effects, no threshold exists such as cancers and genetic mutation. The probability of occurrence is proportional to the dose received. ICRP considers that the chance of contracting fatal cancers will increase by 5/100,000 for 1 mSv of radiation dose absorbed.^{1, 2, 6}

What are the Principles for Radiation Protection?

Any practice that will cause an increased exposure to radiation should be carefully judged according to the three basic radiological protective principles. (1) Justification of practice: the practice should produce more benefit to the exposed individual or society than harm. (2) Optimisation of protection: radiation dose to people should be kept "As Low As Reasonably Achievable" – ALARA. (3) Individual dose limits: ensure that no individual should be exposed to unacceptably high radiation dose. The current regulatory standard for nuclear industry workers is 20mSv/yr and for the general public is 1 mSv/yr.^{2, 3, 4, 5, 6}

What are the Variables in Radiation Protection?

The variables in radiation protection are Time, Distance and Shielding. The less time we are exposed to radiation, the less we receive the dose. The fall in radiation dosage with distance follows the "Inverse Square Law"; i.e. the dose is only one-quarter when the distance from the source is doubled. Shielding: lead sheets or concrete walls are effective in reducing radiation exposure. Furthermore, staying indoors during the passage of a radioactive plume and avoiding consumption of contaminated food and water are important measures to reduce radiation hazards when there is environmental contamination.

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Health Concerns in the On-going Fukushima Nuclear Incident

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Dr. Chor-man LO

Introduction

In the on-going Fukushima Nuclear Power Plant incident, potential radiation hazards to the population around the region includes (1) external contamination by the radioactive plume, (2) irradiation by radiation fallout, and (3) internal contamination by radioactive substances.

Radioactive Plume

From the Chernobyl experience, when there is leakage of radioactivity from any nuclear power plant, krypton and xenon (inert gases which are products from fission and decay of uranium and plutonium) will escape and disperse in the atmosphere. Significant amounts of volatile iodine-131 (I-131) and radioactive caesium will also be released¹. Since iodine and caesium will condense quickly with a fall in ambient temperature, they will eventually deposit onto the ground with the potential of environmental contamination and accumulation in the food chain. Deposition will depend on meteorological conditions (e.g. wind direction and rainfall). In general, deposition decreases quickly with distance from the source. In the United States, the plume exposure pathway Emergency Planning Zone (EPZ) has a radius of 10 miles (16 km) from the reactor site². In Hong Kong, the EPZ is an area 20 km from the site of a nuclear power station³.

In the event of a radiation emergency, the local government should estimate the scale of leakage and monitor the environment so as to give appropriate advice to the population in the vicinity, especially for those inside the EPZ. Before the passage of the plume, people should either be evacuated or seek sheltering.

External contamination is not particularly difficult to manage. When people go outdoors, they should put on long-sleeve clothing and change clothing upon returning home. Clothing should be washed in the washing machine and the person should bathe and wash his hair. In case of raining weather, an umbrella or raincoat should be used to avoid direct contact of rainwater with the body. Hands and face should be washed and the shoes should be left outside the house. In Hong Kong, the Derived Intervention Levels for Decontamination of skin⁴ is 30 Bq/cm².

Irradiation

For the general population, significant irradiation received as a result of radiation incident is minimal unless the person is in close proximity to the source of radiation release. Irradiation effects can be divided into acute radiation syndrome (ARS) and cutaneous radiation injury. For ARS to occur, several conditions should be fulfilled. These conditions include (1) the radiation dose

must be large (at least 0.3 Gray); (2) the dose is usually external; (3) the radiation must be penetrating; (4) the entire body (or a significant part of it) must have received the dose; and (5) the dose must have been delivered in a short time (in terms of minutes). There are four stages of ARS, namely the prodromal stage, latent stage, manifest illness stage, followed by recovery or death. Clinical features in the prodromal stage are very non-specific. The time from exposure to vomiting may be useful for estimating the dose received, i.e. the higher the dose, the sooner vomiting occurs. The earliest and most sensitive test for significant radiation exposure is the absolute lymphocyte count. The rate of decline of the absolute lymphocyte count can be plotted against the Andrews Lymphocyte Nomogram for estimation of prognosis⁵.

Cutaneous radiation injury can occur with doses as low as 2 Gray. Early features are unexplained itching, tingling, transient redness or oedema. Cutaneous radiation injury also evolves in stages, namely the prodromal stage, latent stage, manifest illness stage, third wave of erythema, late effects and finally recovery⁵.

Internal Contamination

We may contract internal contamination via inhalation, ingestion or absorption through wounds or embedded foreign bodies. Decorporation (if feasible) may be necessary if there is a significant amount of internal contamination. For the general population, the government will advise on evacuation or sheltering if they are endangered by the passage of a radioactive plume. Therefore, significant internal contamination via inhalation is rare. Contamination via absorption from contaminated wounds or embedded foreign bodies should be managed with decontamination and surgical removal as appropriate. Protection from ingestion should follow the guidance of the local government. Import of goods from potentially contaminated areas will be checked for radiation hazards. In Hong Kong, the allowable limit of foodstuff for I-131 is 100 Bq/kg⁶.

Safety of Health Care Worker (HCW)

It is natural for HCW to be anxious about their own safety when they are assigned to take care of victims of nuclear and radiation incidents. For external contamination, it can be detected by the Geiger-Muller counter. Moreover, taking off the outer clothing (and wrap in double plastic bags) and washing the hands and face can normally remove 90% of external contamination. In overseas experience, members of the emergency response team were never significantly affected by radiation when they discharge their duties. Concerning patients with internal contamination, the London Polonium-210 poisoning incident in 2006 is a useful illustration. Two hundred and thirty eight HCW were assessed for health effects in



the incident. Seventy six of them were asked to submit urine for further testing. Sixty nine urine samples were tested and none was shown to be affected. A total of 738 urine samples were tested and only 17 patients were found to have significant radiation levels (above 6 mSv) that warranted long term follow-up. None of them were HCW⁷. Lastly, irradiated patients pose no threat to HCW (similar to someone who had undergone x-ray examination). Therefore, HCWs practising universal and radiation precaution under the guidance and supervision of medical physicists should be very safe when they discharge their duties.

Conclusion

For citizens in Hong Kong, the risk of direct adverse effects (external contamination and irradiation) from the radioactive fallout is minimal. Contamination of the food chain is a potential threat and we should trust the

effectiveness of our government in radiation surveillance of imported goods. HCWs should be safe if they practise universal and radiation precautions and work under the guidance of medical physicists.

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Antidotal Treatment for Radioactive Materials

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Dr. Man-li TSE

Introduction

Internal contamination occurs when radioactive materials get into a patient's body. Possible routes are inhalation, ingestion, percutaneous absorption and penetration. Focusing on the recent scenario of this nuclear power plant leakage, the radioactive materials of concern are radionuclides, atoms with unstable nuclei which emit radiation. They get into the human body through inhalation of the contaminated air or ingestion of the contaminated food products. When the absorbed concentration of these radionuclides exceed certain levels, antidote treatment should be considered by a multidisciplinary team that includes radiation specialists, clinical toxicologists and medical doctors from other specialties.

Pharmacological Principles

Strictly speaking, there exists no antidote for radiation injuries. However the term is still borrowed from its toxicological context for the ease of understanding. Decorporation is the more used term which literally means removal (of radioactive materials) from the patient's body. As the radionuclides possess the same pharmacological properties as their non-radioactive counterparts, (for example, radioactive caesium-137 is handled pharmacokinetically by our body in the same way as the usual non-radioactive caesium-133) therefore they are amenable to the same treatment measures as in caesium-133 poisoning.

The principles of decorporation treatment include the following:

- (1) Gastrointestinal decontamination: gastric lavage, laxative and even whole bowel irrigation may be applied in acute ingestion of a significant dose of radioactive materials that presents early.
- (2) Reduced gastrointestinal absorption by saturating the gastrointestinal tract with a physiologically similar chemical.
- (3) Enhanced elimination by physiological manipulation, e.g. increasing urine output, blood acidification and urinary alkalisation.
- (4) Blockage of end organ absorption.
- (5) Enhanced elimination by chelation therapies
- (6) Transformation of radionuclides into less chemically toxic substances to reduce their specific chemical toxicities.

Indication

Indication of decorporation treatment, like most if not all other medical treatments is based on risk-benefit consideration. The first rule-of-thumb is that any medical and surgical emergencies should take the first priority, decorporation should not delay or impede the emergency treatment of such conditions. The second priority is external decontamination if needed in order to prevent secondary contamination as well as any possible ongoing internalisation of the radionuclides on the body surface. After clearance of these two, the decision of decorporation treatment should be considered. It should be balanced among the estimated harm from the internalised radiation, the potential adverse effects from the treatment and the medical resources available in a crisis situation. The radiation dose needs to be assessed by a radiation specialist who should be able to advise on



the type and dose of radionuclides being internalised so that the potential harm to the patient can be estimated. There is no well established threshold radiation level for decorporation. One conservative approach is to use the Annual Limit of Intake (ALI) established for nuclear plant workers as the threshold dose. However at risk groups like pregnant women and children would need special consideration.

Radionuclide-specific Treatment

In the scenario of leakage from a damaged nuclear power plant not in the very close proximity, several radionuclides species are usually released in large amounts. They include the radioactive isotopes of iodine, strontium, caesium, plutonium and uranium. The specific decorporation treatment of each radionuclide will be discussed.

Iodine-131

As form of iodine, iodine-131 is absorbed and concentrated in the thyroid gland for the production of thyroxines making the thyroid gland most vulnerable to its carcinogenic effect. In order to stop the absorption, non-radioactive iodine supplement at high dose in the form of potassium iodide can be used to saturate the thyroid gland. The unabsorbed iodine-131 will then be excreted in the urine. This treatment is most effective if administered shortly before radionuclide exposure. Its effect wanes over hours and is considered useless 12 hours after radioactive iodine internalisation. The usual adult dose is 130mg orally once daily. The dose is reduced to 65mg daily for a 4 to 18 year old, 32.5mg daily for a 1 month to 3 year old and 16.25mg daily for those younger than 1 month old. For patients older than 40 year old, as the risk of radiation-induced thyroid cancers in their expected life span being low, a higher threshold radiation dose is recommended for their treatment. The treatment should be continued when the air and food are free of significant iodine-131 or the patient has been removed to a protected place with uncontaminated food supply. Contraindications for potassium iodide are iodine hypersensitivity, dermatitis herpetiformis and hypocomplementemic vasculitis.

When the treatment window has passed before potassium iodide is available, propylthiouracil can be considered. It is a drug commonly used in the treatment of thyrotoxicosis. It also inhibits the absorption of iodine by the thyroid gland. The usual adult dose is 100mg thrice daily for 8 days.

Caesium-137

Caesium is handled by the body similar to potassium, once inside the body, it will be transported inside cells by the sodium-potassium pump on cell membranes. Insoluble Prussian blue has been successfully used in the treatment for radioactive caesium contamination as well as in non-radioactive caesium poisoning. It significantly reduces the plasma half life of caesium through a several fold increase in the faecal elimination of caesium. The usual dose is 1gm orally thrice daily for three weeks. In severe exposure cases, its dose may be increased up to 12gm daily and for a longer duration. Prussian blue is usually well tolerated with constipation as the commonest reported adverse effect.

Strontium-90

Radioactive strontium once absorbed will be concentrated in bones due to its pharmacological

resemblance to calcium and therefore it increases the risks of bone cancer and leukaemia. Its similarity to calcium is utilised as a principle of treatment. Blood and urine acidification together with calcium supplement is recommended as the decorporation treatment of choice. The usual regime is ammonium chloride 1-2 gm orally four times daily, together with 50ml of 10% calcium gluconate in 500ml dextrose solution via intravenous infusion over 4 hours daily for 6 days. Monitoring of the blood pH, calcium and other electrolyte concentrations are needed. In a case of acute radioactive strontium ingestion which presents early, gastrointestinal decontamination with sodium alginate powder 10gm in water or a big dose of calcium carbonate (5 gm two to four hourly) can reduce strontium absorption.

Plutonium-239

The metal chelator DTPA (diethylene triamine pentaacetic acid) is recommended for the decorporation of radioactive plutonium. Treatment regime starts with calcium DTPA for one to a few doses daily followed by a dose of zinc DTPA daily for several days are usually used. Such a mixed regime is based on the fact that calcium DTPA is more effective than zinc DTPA as least in the first 24 hours after exposure but it also depletes the essential metals in the body like zinc, magnesium and manganese. Both types of DTPA are given as 1gm in 250ml dextrose solution intravenously over 1 hour, once daily. Zinc DTPA is more preferable in the treatment of pregnant women because of the reported higher reproductive outcome risk associated with calcium DTPA. However in case of heavy internal contamination by plutonium, the reproductive risk has to be balanced against calcium DTPA's better effectiveness. Nebulised forms of the two antidotes may also be used for inhalation-only exposures to plutonium within 24 hours. DTPAs should be used cautiously in haemochromatosis, asthma and renal failure as well after repeated dosings.

Uranium-238

Apart from its radioactivity, uranium is also renal toxic. Alkaline urine promotes the formation of the less renal toxic uranium bicarbonate. Urine alkalisation can be achieved by giving 50 to 100 ml 8.4% sodium bicarbonate intravenously in the first half to one hour, then titrate the subsequent infusion rate aiming at a urine pH of 7.5 to 8. Blood pH and potassium need to be monitored. Urine alkalisation by oral intake of sodium bicarbonate is also possible.

Conclusion

The treatment of radioactive material contamination requires the collaboration of a multidisciplinary team of specialists. Treatment decision should be based on risk-benefit considerations. Type of radionuclides, the dose, the route of body entry and the time of exposure are all essential information needed in deciding on the appropriate antidote regime.

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Federation Spring Dinner



To mark the good beginning of the Rabbit New Year, the Federation Family – the Executive Committee Members and the Secretariat enjoyed a delightful evening with some delicious nostalgic cuisines, much fun and laughter on Mar 2, 2011.

The Secretariat would like to express our sincere gratitude to the President, the Officers and the Executive Committee for their kind support and encouragement throughout the past years.

Seminar: Studying in the UK



The Federation was pleased to present our members an informative seminar on the UK Education, jointly organised by the Federation, the British Medical Association (HK) and the British Council. The Seminar was held on Mar 7, 2011 with 2 sessions. First session was conducted by Ms Katherine Forestier, Director of Education and Society, British Council, on the Hong Kong's new academic structure and pathways to studying in the UK at school and university levels and applying to universities in the UK. The second session was conducted by Mr Rob Aldridge, Regional Manager for the Far East, Oxford Brookes University on how to make the right choice of university and course, and how to make a winning application. Much invaluable information and advices were given during the presentation.

We would like to thank our guest speakers Ms Katherine Forestier and Mr Rob Aldridge, the British Medical Association (HK), the British Council and the participants from our member societies for the support to the Seminar!

RTHK 醫學組織聯會時間 (1) - 香港醫訊 / 醫療熱話

Starting from Mar 14, 2011, the Federation was offered a regular weekly time slot from 1pm to 2pm on each Monday on RTHK Radio 1 to feature the various health topics for the general public. The radio programme content is based on the concurrent monthly Medical Diary topics with public-oriented approach delivered by our various Medical Diary editors. While thanking the invitation from Mr Simon Siu of the RTHK Radio 1, the Federation would also like to express our gratitude to the Medical Diary editors and authors for their support. You may go to RTHK Radio website for the programme archives - <http://rthk.hk/index.htm>.



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
<ul style="list-style-type: none"> *MPS – Mastering Professional Interactions *HKMA Dragon Boat Team Practice Session <p>3</p>	<ul style="list-style-type: none"> *HKMA Choir Rehearsal <p>4</p>	<ul style="list-style-type: none"> *HKMA Council Meeting <p>5</p>	<ul style="list-style-type: none"> *Hong Kong Neurosurgical Society Monthly Academic Meeting – Flow Dynamics in Cerebral Aneurysm *HKMA – Central, Western & Southern Community Network - Certificate Course on Dermatology <p>6</p>	<ul style="list-style-type: none"> *FMSHK Officers' Meeting <p>7</p>	<ul style="list-style-type: none"> *Joint Surgical Symposium - Recurrent ENT Disease <p>1</p>	<ul style="list-style-type: none"> *MPS – Mastering Your Risk Workshop <p>2</p>
<ul style="list-style-type: none"> *HKMA Dragon Boat Team Practice Session *HKMA Certificate Course on Family Medicine 2011 *HKMA Snooker Tournament <p>10</p>	<ul style="list-style-type: none"> *HKMA Choir Rehearsal *Private-public Interface – Bridging the Gap between the Careers: Aspects of Private Urological Practice that may be Useful to Urologists in Public Sector <p>11</p>	<ul style="list-style-type: none"> *HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2011 - What is IMRT? <p>14</p>	<ul style="list-style-type: none"> *HKMA Shatin Doctors Network - Treatment and Prevention of Cerebrovascular Disease: An Update <p>15</p>	<ul style="list-style-type: none"> *HKMA Kowloon East Community Network - Lecture Series on BPH & Common Urological Diseases for Men after 50s <p>7</p>	<ul style="list-style-type: none"> *Refreshers Course for Health Care Providers 2010/2011 *MPS - Mastering Adverse Outcomes Workshop *Fifth Meeting of Medical History Interest Group <p>9</p>	<ul style="list-style-type: none"> *HKMA - KLN East Community Network; HA - UCH; HKCFP - CME Course for Health Personnel 2011 *MPS - Mastering Professional Interactions *Youth Committee - Chocolate Making Workshop <p>16</p>
<ul style="list-style-type: none"> *HKMA Dragon Boat Team Practice Session *HKMA Snooker Tournament <p>17</p>	<ul style="list-style-type: none"> *HKMA Choir Rehearsal <p>18</p>	<ul style="list-style-type: none"> *FMSHK Executive Committee Meeting *HKMA - Kln West Community Network - Updated Information for Cervical Cancer Vaccine <p>19</p>	<ul style="list-style-type: none"> *HKMA - Central, Western & Southern Community Network - Certificate Course on Dermatology <p>20</p>	<ul style="list-style-type: none"> *HKMA - NT West Community Network - Use of Vaginal Probiotic in Clinical Practice *HKMA - Kln West Community Network - Management of Haematuria and Urinary Stone Disease *HKFMS Foundation Meeting <p>28</p>	<ul style="list-style-type: none"> *HKCC 19th Annual Scientific Congress <p>22</p>	<ul style="list-style-type: none"> *MPS - Mastering Your Risk Workshop <p>23</p>
<ul style="list-style-type: none"> *HKMA Dragon Boat Team Practice Session <p>24</p>	<ul style="list-style-type: none"> *HKMA Choir Rehearsal <p>25</p>	<ul style="list-style-type: none"> *HKMA - Kln West Community Network - Updated Information for Cervical Cancer Vaccine <p>19</p>	<ul style="list-style-type: none"> *HKMA - Central, Western & Southern Community Network - Certificate Course on Dermatology <p>20</p>	<ul style="list-style-type: none"> *HKMA - NT West Community Network - Use of Vaginal Probiotic in Clinical Practice *HKMA - Kln West Community Network - Management of Haematuria and Urinary Stone Disease *HKFMS Foundation Meeting <p>28</p>	<ul style="list-style-type: none"> *HKCC 19th Annual Scientific Congress <p>22</p>	<ul style="list-style-type: none"> *MPS - Mastering Your Risk Workshop <p>23</p>



Date / Time	Function	Enquiry / Remarks
1 8:00 am – 9:00 am FRI	Joint Surgical Symposium - Recurrent ENT Disease Organisers: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Chairman: Prof. William I. WEL, Speakers: Dr. Victor TO & Dr. Raymond TSANG, Venue: Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 Fax: 2892 7511 1 CME Point (Active)
2 2:00 pm SAT	MPS – Mastering Your Risk Workshop Organiser: The Hong Kong Medical Association, Speaker: Dr. Andy CHEUNG, Venue: Eaton Hotel	Miss Viviane LAM Tel: 2527 8452 2.5 CME Points
3 2:30 pm SUN	MPS – Mastering Professional Interactions Organiser: The Hong Kong Medical Association, Speaker: Dr. Justin CHENG, Venue: Central	Miss Sophia LAU Tel: 2527 8285 2.5 CME Points
4 (10,17,24) MON 8:00 pm (11,18)	HKMA Dragon Boat Team Practice Session Organiser: The Hong Kong Medical Association, Chairman: Dr. CY YAM & Dr. PY CHENG, Venue: Sai Kung or Stanley Main Beach HKMA Choir Rehearsal Organiser: The Hong Kong Medical Association, Chairman: Dr. YS CHAN & Dr. YM NG, Venue: GPI, HKCC	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285 Ms. Candy YUEN Tel: 2527 8285
7 8:00 pm – 10:00 pm THU	FMSHK Officers' Meeting Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345
9 2:30 pm SAT 2:30 pm 3:30 pm – 5:30 pm	Refresher Course for Health Care Providers 2010/2011 Organiser: The Hong Kong Medical Association, Chairman: Dr. CM CHENG, Speaker: Ms. Eliza WONG, Venue: OLMH MPS - Mastering Adverse Outcomes Workshop Organiser: The Hong Kong Medical Association, Speakers: Dr. Anthony FUNG & Dr. Patrick AU, Venue: Central & Empire Hotel Fifth Meeting of Medical History Interest Group Organiser: Hong Kong Museum of Medical Sciences Society, Chairperson: Prof. Rosie YOUNG, Speaker: Prof. Eng Kiong YEOH, Venue: Lecture Theatre, M/F, Block M, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon	Miss Sophia LAU Tel: 2527 8285 2 CME Points Miss Sophia LAU & Miss Joey LEE Tel: 2527 8285 2.5 CME Points Tel: 2549 5123 Email: info@hkmmcs.org.hk 0.5 - 1 CME Point
10 2:00 pm SUN 2:00 pm (17)	HKMA Certificate Course on Family Medicine 2011 Organiser: The Hong Kong Medical Association, Chairman: Dr. CM Cheng, Speakers: Dr. CHOI Kin, Gabriel & Dr. CHAN Kwok Wing, Fredrieck, Venue: Queen Elizabeth Hospital, Kowloon HKMA Snooker Tournament Organiser: The Hong Kong Medical Association, Chairman: Dr. R CHEUNG, Venue: Prat Billiard Club	Miss Sophia LAU Tel: 2527 8285 3 CME Points Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
11 7:30 pm – 8:30 pm MON	Private-public Interface – Bridging the Gap between the Careers: Aspects of Private Urological Practice that may be Useful to Urologists in Public Sector Organiser: Hong Kong Urological Association, Chairman: Dr. SUN Wai Ho, Speakers: Various, Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon	Dr. HUNG Hing Hoi / Ms. Tammy HUNG Tel: 2958 6006 / 9609 6064 Fax: 2958 6076 / 8344 5115 1 CME Point
12 8:00 pm TUE	HKMA Council Meeting Organiser: The Hong Kong Medical Association, Venue: Wanchai	Ms. Christine WONG Tel: 2527 8285
13 7:30 am WED 1:00 pm (27)	Hong Kong Neurosurgical Society Monthly Academic Meeting – Flow Dynamics in Cerebral Aneurysm Organiser: Hong Kong Neurosurgical Society, Chairman: Dr. KM LEUNG, Speaker: Dr. LAM Siu Kei, Samuel, Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon HKMA - Central, Western & Southern Community Network - Certificate Course on Dermatology Organiser: HKMA CW&S Community Network, Chairmen: Dr. TSANG Chun Au & Dr. CHAN Hau Ngai, Kingsley, Speakers: Dr. WONG Sai Siong & Dr. CHAN Hin Lee, Henry, Venue: HKMA Central Premises	Dr. Gilberto LEUNG Tel: 2255 3368 Fax: 2818 4350 Miss Carman WONG Tel: 2527 8285 1 CME Point
14 1:00 pm THU 2:00 pm	HKMA Kowloon East Community Network - Lecture Series on BPH & Common Urological Diseases for Men after 50s Organiser: HKMA Kowloon East Community Network, Chairman: Dr. KK AU, Speaker: Dr. YUNG Yee Ping, Venue: Lei Garden Restaurant, Shop L5-8, APM, No. 418 Kwun Tong Road, Kwun Tong, Kowloon HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2011 - What is IMRT? Organiser: The Hong Kong Medical Association, Chairman: Dr. CM CHENG, Speaker: Dr. KWAN Wing Hong, Venue: Central	Miss Carman WONG Tel: 2527 8285 1 CME Point Miss Sophia LAU Tel: 2527 8285 1 CME Point
15 1:00 pm FRI	HKMA Shatin Doctors Network -Treatment and Prevention of Cerebrovascular Disease: An Update Organiser: Shatin Doctors Network, Chairman: Dr. WK MAK, Speaker: Dr. LEUNG Ho Wan, Venue: Shatin	Miss Candice TONG Tel: 2527 8285 1 CME Point
16 1:30 pm SAT 2:00 pm 4:00 pm	HKMA - KLN East Community Network; HA - UCH; HKCFP - CME Course for Health Personnel 2011 Organiser: HKMA Kowloon East Community Network; HKCFP & UCH, Chairman: Dr. KK AU, Speaker: Ms. Natalie CHAN, Venue: Lecture Theatre, G/F., Block F, United Christian Hospital, Kowloon MPS - Mastering Professional Interactions Speaker: Dr. Andy CHEUNG, Venue: Eaton Hotel Youth Committee - Chocolate Making Workshop Organiser: The Hong Kong Medical Association, Chairmen: Dr. J. PONG & Dr. H. SIN, Venue: VERO Lounge	Ms. Gary WONG Tel: 3513 4821 1.5 CME Points Miss Sophia LAU Tel: 2527 8285 2.5 CME Points Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
19 8:00 pm – 10:00 pm TUE 1:00 pm	FMSHK Executive Committee Meeting Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong HKMA - Kln West Community Network - Updated Information for Cervical Cancer Vaccine Organiser: HKMA Kln West Community Network, Speaker: Dr. FONG Yeung, Francois, Venue: Panda Hotel, Tsuen Wan	Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345 Miss Candice TONG Tel: 2527 8285
28 1:00 pm THU	HKMA - NT West Community Network - Use of Vaginal Probiotic in Clinical Practice Organiser: HKMA NTW Community Network, Chairman: Dr. Erica HUEN, Speaker: Dr. YEO Lee Kung, Evelyn, Venue: Maxim's Palace Chinese Restaurant, Tuen Mun Town Hall, 3 Tuen Hi Road, Tuen Mun, N.T.	Miss. Carman WONG Tel: 2527 8285 1.5 CME Points



Date / Time	Function	Enquiry / Remarks
28 THU 1:00 pm 8:00 pm – 10:00 pm	HKMA - Kln West Community Network - Management of Haematuria and Urinary Stone Disease Organiser: HKMA Kln West Community Network, Speaker: Dr. TO Kim Chung, Venue: Panda Hotel, Tsuen Wan	Miss Candice TONG Tel: 2527 8285
	HKFMS Foundation Meeting Organiser: HKFMS Foundation Limited, Venue: Lecture Hall, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345
29 FRI 8:00 am	HKCC 19th Annual Scientific Congress Chairman: Dr. CS CHIANG, Venue: Sheraton Hotel & Towers, Kowloon	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285

Courses / Meetings

12-14/5/2011	18th Asian Congress of Surgery & 37th Philippine College of Surgeons Mid-year Convention Organiser: Asian Surgical Association, Venue: Waterfront Cebu City Hotel & Casino, Lahug, Cebu City, Philippines, Enquiry: Congress Secretariat, Tel: (632) 9274973-74; (632) 9281083; (632) 9292359, Fax: (632) 9292297, E-mail: secretariat@acs2011.org, Website: http://www.acs2011.org
12-15/5/2011	第18屆世界美容醫學大會 Organiser: Union International de Medicine Esthetique (UIME), Chairman: 劉洪臣先生, Venue: 中國北京市朝陽區北辰東路8號中國北京國際會議中心, Enquiry: Ms. Echo LEUNG, Tel: 3575 8600, Fax: 2301 2414, Email: aiam_hk@yahoo.com, Website: http://www.wcam2011.org
22/5/2011	2011 Paediatric Update No. 1 Seminar on Infant and Young Child Feeding Organiser: Hong Kong College of Paediatricians, Chairman: Dr. WONG Sik Nin & Dr. Shirley LEUNG, Speakers: Various, Venue: Lecture Theatre, Hospital Authority Head Office, Enquiry: Ms. Vanessa WONG, Tel: 2871 8773, Fax: 2785 1850
16/7/2011	Hong Kong Surgical Forum – Summer 2011 Organiser: Department of Surgery, The University of Hong Kong; Queen Mary Hospital & Hong Kong Chapter of American College of Surgeons, Venue: Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam, Hong Kong, Enquiry: Forum Secretary, Hong Kong Surgical Forum, Tel: 2255 4885 / 2255 4886, Fax: 2819 3416, Email: hksf@hku.hk, Website: http://www3.hku.hk/surgery/forum.php

Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

Date	Course No	Course Name	Target Participants	CME/CNE
1/4/2011 - 13/5/2011	C173	Certificate Course on Management of Common Psychiatric Disorders 2011	Medical and Health Professionals	9 CNE Points; CME/CPD Accreditation in application
6/4/2011 - 11/5/2011	C176	Certificate Course on Paediatric Nephrology 2011	General Practitioners, Health Care Providers and Public Who Are Interested in Common Kidney Problems in Children	9 CNE Points; CME/CPD Accreditation in application
5/5/2011 - 9/6/2011	C172	Certificate Course on Current Management of Common Head & Neck Cancers	Medical, Health Professionals and General Public	9 CNE Points; CME/CPD Accreditation in application
12/7/2011 - 16/8/2011	C178	Certificate Course on Occupational Hygiene Practice	Healthcare Workers	9 CNE Points; CME/CPD Accreditation in application



Society News

News from Member Societies

- The Hong Kong Orthopaedic Association**
Updated office-bearers for the year 2011 - 2012 are as follows: President: Dr. Y.L. LEE; Honorary Secretary: Dr. W.L. TSANG; Honorary Treasurer: Dr. Raymond N.M. WONG
- The Hong Kong Society of Professional Optometrists**
Updated office-bearers for the year 2011 - 2012 are as follows: President: Dr. Larry NG
External Secretary: Dr. Anderson TAM; Treasurer: Miss Victoria LAW
- The Hong Kong Society of Sleep Medicine**
Updated office-bearers for the year 2011 - 2012 are as follows: President: Dr. Kah-lin CHOO; Honorary Secretary: Dr. Jamie Chung-mei LAM; Honorary Treasurer: Dr. Samson Yat-yuk FONG

The FMSHK would like to send its congratulations to the new office-bearers and look forward to working together with the societies

Welcome New Members

- The Hong Kong Burns and Wound Healing Society Limited
- The Hong Kong Paediatric Dermatology Society Limited

The FMSHK would like to welcome the above organisation as members of the Federation.



Answer to Radiology Quiz

Diagnosis:

Rt staghorn stone
Lt medullary nephrocalcinosis
(Patient has hyperoxaluria.)

Radiological Findings:

AXR:

1. showing Rt-sided staghorn stone.
2. Multiple tiny calcifications with the appearance of 'bundle of grapes' are seen over the Lt kidney.

5min post-contrast IVU images:

1. Marked delay in excretion of contrast in the Rt kidney, due to obstruction by the Rt staghorn stone.
2. Normal excretion of Lt kidney. Multiple small calcifications are seen evenly distributed over the pyramids of all the Lt renal calyces.

Discussion:

Nephrocalcinosis is a condition of diffuse, evenly distributed fine calcifications within the renal tubules or cortex as seen on AXR, by US or on CT. Usually nephrocalcinosis is confined to the medullary regions of the kidneys. More rarely, calcifications are noted within the renal cortex.

Medullary nephrocalcinosis is characterised by a wedge-shaped pattern of fine, or occasionally coarse, calcification which corresponds to the medullary pyramids. The pyramids become diffusely involved, but in the early phases only several pyramids may show calcific deposits. This abnormality is associated with recurrent renal calculi.

Medullary nephrocalcinosis is a manifestation of metabolic disorder. Renal tubular acidosis (RTA) is the most common cause. The diagnosis is usually made in the early months of life or during childhood. If untreated, renal damage and progressive renal failure will result from nephrocalcinosis and hypocalcaemia.

Primary hyperoxaluria is another cause. The calcifications are coarser and denser than RTA. In the fulminant infantile variety, the calcifications are both cortical and medullary.

Other disorders producing medullary nephrocalcinosis include: hypercalciuria, primary hyperparathyroidism, hypervitaminosis D, immobilisation, endogenous or exogenous Cushing syndrome, sarcoidosis or ketogenic diet. Renal vein thrombosis, idiopathic hypercalcaemia, and hypercalciuria without hypercalcaemia may produce nephrocalcinosis. Nephrocalcinosis and nephrolithiasis are also seen in preterm infants with prolonged furosemide treatment and calcium supplements.

Dr. Wendy LAM

Consultant Radiologist, Department of Radiology,
Queen Mary Hospital

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