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The Cover Shot

Mother and child

攝於雲南。幸運地在一條小村路上捕捉到一位少數民族 (哈尼族) 少婦背着幼兒回家時回望的神情。

Dr. Kin-ming WONG
MBBS(HK), DFM(CUHK), DOM(CUHK), DDME(CUHK)

香港醫訊

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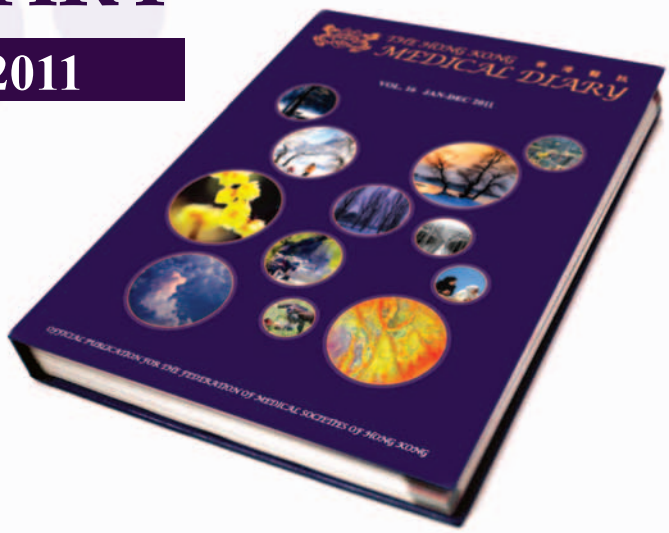

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Editorial

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Editor

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The year 2012 is a very dramatic year for the specialty of Obstetrics and Gynaecology. The delivery rate this year will hit a historical high because of the Year of the Dragon and the huge influx of Non-Entitled Persons (NEP), mostly from the China mainland. In the year 2001, there were only 48,219 deliveries in Hong Kong, of which only 620 were mothers from the mainland (1.3%). In 2010 there were 32,635 mothers from the mainland delivered in Hong Kong, making up 37% of the total deliveries of 88,323. The majority of these babies were born in private hospitals, thus flourishing the 'maternity businesses' in the private sector. The following problems were identified within our specialty:

1. The maternity service units of HA hospitals were under heavy stress, especially the neonatal ICU services.
2. The maternity service units of private hospitals were under heavy demand, making booking of local mothers for delivery beds very difficult.
3. Training of OG trainees in HA units was compromised because of the heavy workload for maternity services. Some gynaecological operations had to be postponed because of the limited operation theatre time.
4. There was a great exodus of OG specialists and midwives from HA hospitals to the private sector, probably because of better working conditions and 'good business'.
5. Expansion of maternity services in private hospitals to accommodate the demand from NEP mothers, thus making non-obstetric services a lower priority.

I do not propose to discuss the impact of NEP mothers on the economical and social resources of Hong Kong. This will be left to the politicians and the government to consider. However, it had been announced that with the new administration coming to office in July 1, 2012, there will be zero quota for the NEP mothers from the mainland to deliver in Hong Kong after January 2013. The immediate impact on the OG specialty is obvious. For the HA hospitals, we will be expecting more obstetric emergency admissions by NEP mothers from the mainland. For the private sector, this will mean a significant reduction in obstetric admissions and hence a decrease in revenue. How to cope with this new era is a challenge to the hospital administrators and the practising OG specialists. Future planning on service provisions, quality of OG training and manpower requirements have to be carefully studied to cope with the new government policy. I think this is a good opportunity for the stake holders to sit back and reconsider the core value of OG services in Hong Kong.

In this July issue of the Medical Diary, we have experts from the OG specialty to write on some new developments. HPV vaccination has been in practice for some years. New data from population studies in Australia and United Kingdom showed a significant decrease in genital warts and high grade cervical squamous neoplasia. This is another new advancement to prevention of cervical cancer after the implementation of routine Pap smears. Dr Tam Kar-fai will give us a new update on

the HPV vaccines and its applications. With improved treatment of cancer patients (surgery, chemotherapy and/or radiotherapy) we are seeing more and more young cancer survivors wishing for having babies in future. How to help these young patients to preserve their future fertility is highlighted by Professor Ernest Ng's article. On the obstetric side, Dr Lau Tze Kin wrote on new and non-invasive methods of prenatal diagnosis of foetal Down's syndrome with the recent advancement of molecular studies. A lot had been discussed on the storage and use of cord blood stem cells (**haematopoietic stem cells, HSC**). Dr Xiaoai Zhang discussed on emergent therapeutic applications of human umbilical mesenchymal stem cell (**MSC**) which is a new source of stem cells. This opens a new area for tissue repair and restoration medicine. All the articles are written for both OG and non-OG practitioners. Please enjoy.

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Multifunction Room I *(Max 15 persons)*	150.00	105.00	225.00	250.00	175.00	375.00
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Prenatal Screening and Diagnosis of Foetal Down Syndrome (Trisomy 21)

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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 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 July 2012.

Background

The objective of this article is to provide an update on the latest development in the prenatal screening and diagnosis of foetal Down syndrome, or Trisomy 21.

The incidence of Down syndrome is about 1 in 700 live births. Individuals with Down syndrome have a particular set of facial features, impairment of cognitive ability with an average IQ of about 50, and sometimes other congenital anomalies such as heart defects. Down syndrome is a non-fatal chromosomal disorder. Some parents consider that the birth of a child with Down syndrome will cause significant physical, psychological, social and financial stress and morbidity to the family, while others report a very positive effect on the family life. Therefore, there is a constant debate on the ethics of prenatal screening and diagnosis of foetal Down syndrome. Nonetheless, over 86% of the local pregnant women responded to a questionnaire study that they would have an abortion if they had an affected pregnancy[1], while based on my clinical experience, over 95% of those who had an affected pregnancy confirmed by prenatal diagnosis had chosen pregnancy termination. Therefore, the reality is that prenatal screening and diagnosis of foetal Down syndrome has become an integral part of obstetric care in many societies, including Hong Kong.

Diagnostic Tests

A definitely prenatal diagnosis of foetal Down syndrome requires the cytogenetic study of foetal cells obtained from an invasive procedure, either amniocentesis or chorionic villus sampling (CVS). Table 1 shows the important differences between these 2 procedures. Both amniocentesis and CVS are accurate procedures for the prenatal diagnosis of Down syndrome. In general, CVS is a more difficult procedure, requiring more skills. Also, confined-placental-mosaicism occurs in about 1% of cases, which might require further amniocentesis to exclude foetal mosaicism. However, from the perspective of prenatal diagnosis of Trisomy 21 only, there is no real advantage of amniocentesis over CVS. The major advantage of CVS is that it is the only safe invasive test that can be performed in early pregnancy, allowing early diagnosis and intervention, and hopefully lowers maternal morbidities.

The major risk of these invasive tests is procedure-related abortion. The estimated risk of amniocentesis is between 0.5 to 1%[2]. Many patients or even health care providers assume that CVS, as that requires more skills, is more risky. However, many studies have shown that CVS, when performed by experienced operators, is associated with the same incidence of abortion rate[3]. Unfortunately, the risk would be higher if performed by inexperienced CVS operators. Therefore, in real clinical situations, the choice between CVS and amniocentesis is usually determined by the gestation at which the pregnant women require the test, how quickly they want to know the answer, and the experience of the operators.

Table 1. Comparison between amniocentesis and chorionic villus sampling (CVS).

	Amniocentesis	CVS
Gestation of test	16-20 week	11-13 week
Skill required	Minimal	High
Approach	Transabdominal	Most commonly transabdominal
Commonly used needle size	22G	17-20G
Local anaesthesia	Usually not required	Usually needed
Pass through uterus	Needed	Needed
Pass through gestational sac	Needed	Not required
Risk of abortion	1 in 100 to 200	1 in 100 to 200
Possibility of confined placental mosaicism	No	Yes

It is important to note that amniocentesis or CVS simply refers to the procedure through which foetal samples are obtained. The commonest laboratory test performed on these samples is "karyotyping", which enables the detection of aneuploidies and large chromosomal rearrangements. Karyotyping is a highly acute test, and has been considered as the gold standard for chromosomal disorders for many years. Unfortunately, this test requires prior cell culture, and therefore the reporting time is long, usually between 2-3 weeks. Also, culture failure occurs in 2-4 per thousand cases. Nowadays, it is a common practice to perform the "Rapid Karyotyping" on un-cultured samples by either FISH (Fluorescence In Situ Hybridisation) or QF-PCR (Quantitative Fluorescent Polymerase Chain Reaction) techniques. Rapid karyotyping enables the exclusion or detection of common aneuploidies involving chromosome 13, 18, 21, X and Y, within 24-48 hours. Rapid karyotyping is highly accurate for Trisomy 13, 18 and 21. False positive results almost never occur.

Due to technical limitations, rapid karyotyping does not exclude mosaicism, aneuploidy affecting other chromosomes, or chromosomal rearrangements. It is worth-noting that up to two thirds of "abnormalities" detected by conventional but not rapid karyotyping were regarded as of no clinical significance, such as balanced translocations[4]. Nonetheless, it is still a common practice to perform both rapid and conventional karyotyping, the former for a quicker result on the important disorders while the later to ensure a complete chromosomal assessment. This completeness of study is also what our pregnant women want[5].

Conventional Screening Tests

Although invasive tests and karyotyping enable the definitive diagnosis of foetal Down syndrome, it cannot be offered to the general obstetric population because the overall disease incidence of 1 in 700 can hardly justify a procedure with up to 1% of abortion risk. Over the past decades, many screening tests have been developed to assist obstetricians in identifying the high-risk group for whom a diagnostic test is justifiable. Table 2 summaries the commonly used one-step screening tests for foetal Down syndrome[6]. Maternal age alone has been used for many years as the sole screening test based on the well-know association between Down syndrome and advanced maternal age. However, it is a very poor screening test with a detection rate (DR) of only 30%. The second trimester biochemical screening test developed in the 1980s increased significantly the DR to 60-70%. However, the nuchal translucency (NT)-based screening strategy has gradually gained worldwide acceptance as the best approach because of the high DR of around 90%[7]. There are many proposed variations, combining these individual tests in the form of "sequential", "integrated" or "contingent" tests. Such combinations are too complicated and therefore will not be discussed further here. In Hong Kong, Down screening has been widely adopted in the private sector for many years, and the Hospital Authority has incorporate this into its obstetric service two year ago.

Table 2. Detection rate (DR) at a 5% False Positive Rate (FPR) for commonly used one-step Down syndrome screening strategies. All strategies combine with maternal age.

	Detection rate
Maternal age alone	30%
Second trimester (Maternal serum biochemical)	
Double or Dual test: AFP + total or free ß hCG	65%
Triple test: AFP + total or free ß hCG + uE3	70%
Quadruple test: AFP + total or free ß hCG + uE3 + inhibin A	80%
First trimester	
Maternal serum biochemical: PAPP-A + free ß hCG	70%
Sonographic: NT	80%
First trimester combined screening: NT + PAPP-A + free ß hCG	90%

AFP: alpha-fetoprotein
hCG: Human chorionic gonadotropin
uE3: Unconjugated estriol
PAPP-A: Pregnancy associated plasma protein A
NT: Nuchal translucency

The principle of the screening test is to divide the population into a large "low-risk" group for whom the risk of being affected is low and could be reassured, and a small "high-risk" group for whom a diagnostic test should be considered. There are some essential points that should be considered when offering these screening tests.

Firstly, the high DR of First Trimester Combined screening is achieved only with proper training and continuous quality control, both for the doctors who perform the sonographic measurements and the laboratories performing the biochemical assay[8]. Virtually all international and national guidelines require that sonographers who perform NT scan should be accredited and certified, and all laboratories providing biochemical assay for Down screening should follow specific quality assurance. In Hong Kong, only 45% of those who perform NT scan are accredited by a recognised body, and only 33% of relevant laboratories participate in external quality assurance programme specific to Down syndrome screening[9]. A poorly performed screening test not only reduces the DR, but also increases the false positive rate (FPR), resulting in more invasive tests and foetal losses.

Secondly, the NT scan could be time-consuming, depending on the position of the foetus at the time of scanning. Therefore, there is no short cut to quality, and enough time must be allocated for the proper measurement of NT. The test must be performed only within 11 to 13+6 week with a foetal crown-rump length between 45-84mm. Figure 1 is a typical image on which the nuchal translucency is measured.

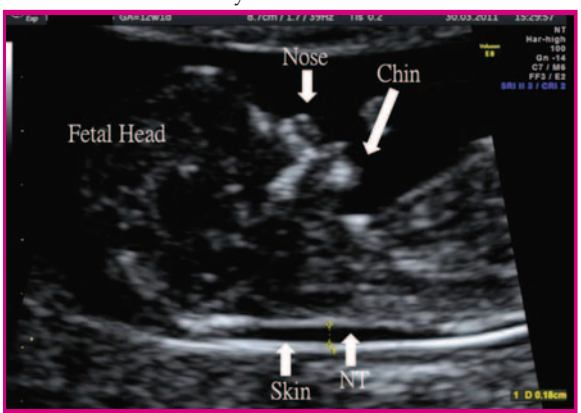

Figure 1. Measurement of nuchal translucency (NT) requires a highly magnified image, including the fetal head and upper thorax only, performed at a gestation between 11- 13+6 week. The boarders of the fluid collection underneath the fetal skin were clearly delineated so that accurate measurement can be made.

Thirdly, all current screening tests are associated with a significant false positive rate, being 5% for most of the strategies. Positive Predictive Value (PPV) is the chance of being affected when one is screened positive. The PPV is affected by the DR, FPR as well as the prevalence of the condition in the population being screened. Table 3 shows how PPV changes when these parameters vary. For the first trimester combined screening with 90% DR and 5% FPR, the PPV was only 1 in 29 and 1 in 12 among the general and high risk populations with a prevalence of 0.2% and 0.5% respectively. Therefore, the majority of the "screened-positive" or "high-risk" cases are in fact normal. This large number of false alarms does create enormous amount of anxiety and "unnecessary" interventions.

Fourthly, even with a detection rate of 90%, many screened-negative pregnant women are still worry. Our previous study have shown that 67% and 59.8% of pregnant women would prefer a definitive answer

by amniocentesis instead of a screening test with 90% detection rate if the amniocentesis-related abortion is 0.5% and 1% respectively[10]. This explains the high proportion of pregnant women who are still anxious to look for more reassurance after a negative Down syndrome screening test.

Table 3. The chance of having an affected fetus given a positive screening test result, the Positive predictive value (PPV), is affected by the prevalence of the condition in the test population, the detection rate and the false positive rate (FPR).

	PPV	
	Prevalence of 0.2%	Prevalence of 0.5%
DR (for 5% FPR)		
60%	2.35% (1 in 43)	5.69% (1 in 18)
80%	3.11% (1 in 32)	7.44% (1 in 13)
90%	3.48% (1 in 29)	8.29% (1 in 12)
100%	3.85% (1 in 26)	9.13% (1 in 11)
FPR (for 100% DR)		
5.00%	3.85 (1 in 26)	9.13% (1 in 11)
3.00%	6.26 (1 in 16)	14.35% (7.0)
1.00%	16.7% (1 in 6.0)	33.4% (1 in 3.0)
0.50%	28.6% (1 in 3.5)	50.1% (1 in2.0)
0.25%	44.5% (1 in 2.3)	66.8% (1 in1.5)
0.10%	66.7% (1 in 1.5)	83.4% (1 in 1.2)

Lastly, because of all these worries, many pregnant women perform multiple screening tests, either the same form of test by different doctors and/or laboratories, or different forms of tests at different gestation ages. If a pregnant woman wants to perform multiple screening tests, these test results should be "Integrated" to take into account of their inter-dependences, which require specific risk-assessment algorithm and software. Such a formal integration of results, unfortunately, is not commonly adopted in clinical practice. Pregnant women usually simply have multiple tests and interpret each of the results in isolation. This is a very inefficient way of screening, without much improvement in DR but a significant increase in the FPR. This should be discouraged.

Non-invasive prenatal diagnosis and screening (NIPD)

Many of our pregnant women worry about the risk of abortion, and yet are not comfortable with the 90% DR of the best screening test in common use. There is a continuous drive to develop a diagnostic test without risks, or a screening test with better performance.

For decades, researchers have been trying to develop effective ways to isolate, purify and identify the few foetal cells present in the maternal circulation, at a concentration of about 1-6 foetal cells per ml of maternal blood[11]. Although occasional successful molecular diagnoses have been reported, the largest collaborative study including 2774 participants showed that at least one foetal cell could only be detected in 41.4% of samples from women carrying a non-trisomy 21 foetus, with a false positive rate of 0.6%[12]. Such a performance was far from acceptable, and this approach of non-invasive prenatal diagnosis (NIPD) has been described as a 'dead duck'[13].

On the other hand, research in the last decade on cell free foetal DNA (cffDNA) has revolutionised our understanding in non-invasive prenatal diagnosis. The presence of cffDNA in the maternal circulation was first reported only 15 years ago in 1997 by Lo et al[14], who convincingly demonstrated the presence of Y-chromosomal DNA sequences derived from a male foetus in the maternal plasma and serum by simple conventional PCR method.

Using real-time PCR system, foetal DNA has been found to constitute 3.4% of all cell-free DNA in maternal plasma during the late first to mid-second trimester, and this percentage rises with advancing gestation to 6.2% at term[15]. Recent study with more precise qualitative methods suggested that the fractional concentration of ccfDNA is as high as 10%. cffDNAs are rapidly cleared from the maternal circulation, with a mean half-life of 16.3 min, and become undetectable in the maternal serum by day 1 after delivery[16]. The fact that, unlike foetal cells, cffDNA does not persist in the maternal circulation after delivery is important from the point of view of prenatal diagnosis in women with prior pregnancies.

It was found that the whole human genome is equally represented in the plasma DNA of pregnant women[17]. Therefore, if the foetus has Down syndrome, there will be more DNA fragments from chromosome 21 getting into the maternal plasma, resulting in a slight but significant elevation of the total chromosome 21 concentration compared to those carrying a normal foetus. The availability of next generation sequencing technology (or known as massively parallel sequencing) enables a precise detection of such a small difference. Essentially, this new technology enables the sequencing of millions of DNA fragments in one single experiment on a glass slide. After sequencing, these millions of fragments with known genetic codes will be compared against the human genome to identify their origins – from which chromosome they come from. Since millions of fragments are counted, the estimated relative concentration of chromosome 21 is highly precise, and any deviation from normal can be detectable.

The successful NIPD of foetal aneuploidy by maternal plasma DNA sequencing was first reported by two independent research groups almost simultaneously in 2008[18-19]. This was quickly confirmed to be a highly accurate, repeatable and reproducible test by many research groups. Table 4 is a summary of the reported performance for the NIPD of foetal Trisomy 21[20-25]. It is beyond doubt that this new test is not yet a diagnostic test but is a highly efficient screening test with a DR of over 99% and a FPR of below 1%.

Table 4. Summary of published report on prenatal detection of fetal Down syndrome by maternal plasma DNA sequencing.

	Case number		Detection rate	False positive rate
	Trisomy 21	Control		
Chiu RWK et al[20]	86	314	100%	97.9%
Sehnert AJ et al[21]	13	34	100%	100%
Ehrich M et al[22]	39	410	100%	100%
Palomaki GE et al[23]	212	1471	98.6%	99.8%
Lau TK et al[24]	11	76	100%	100%
Bianchi DW et al[25]	89	404	100%	100%
Total	450	2709	99.3%	99.7%

Recently, this test has been put into clinical use, starting from China Mainland, Hong Kong and the United States under different names of NIFTY, SafeT21, and MaterniT21. Based on our early experience, there are a few points worth noting.

First, many health care providers and pregnant women have limited knowledge on this test. Therefore, this new test cannot be considered as a simple blood test, but should be integrated with a thorough pre-test counselling and assessment including ultrasound scan.

Second, this test must not be considered as a diagnostic test. Even though the DR is over 99%, pregnant women must accept the very small chance of false negative. On the other hand, even though the FPR is very low, a positive screening result cannot be interpreted as diagnostic, and must be confirmed by karyotyping. In Table 3, it is clear that even for a screening test with 100% DR and 0.1% (1 in 1000) FPR, the positive predictive value will still be only 83% even among the high risk population (i.e. 1.5 out of 10 positive case will still be normal). It is highly likely that with further refinement, the FPR will be even lower. But until the FPR is proven to be 0%, pregnancy termination should not be offered to any one with a positive result without confirmation by karyotyping.

Third, there is increasing evidence that this NIPD test is also highly efficient for the screening of Trisomy 13 and 18[26-27]. In addition, aneuploidies of sex chromosomes might be detectable by this test. In a small study, all 4 cases of Turner syndrome and 1 case of Klinefelter syndrome were correctly identified[23], while in a larger study, 15 of the 16 cases of Turner syndrome were correctly detected[8]. It is necessary to provide adequate pre-test counselling to pregnant women what conditions are included in the test.

Fourth, many pregnant women are keen to know the foetal sex, simply for better early preparation for the arrival of their babies. However, there is always a possibility of misuse by some for sex selection. Currently, foetal sex is not reported by any of test providers.

Fifth, due to the lack of clinical data, this new test cannot be used in multiple pregnancies at present. Having said that, it is almost certain that this test will work equally well in multiple pregnancies. We just have to wait for studies and data to confirm that.

Lastly, some have concerns that all studies so far were performed in high-risk populations and therefore this test should not be used in low risk population. However, we all know that the performance of a screening test is measured by its DR and FPR, which are prevalence independent. It is the PPV and therefore cost-effectiveness that are prevalence-dependent. Therefore, there is no reason why this test should be kept away from the general obstetric population, provided that proper pre-test counselling is provided.

Conclusion

Over the last 2 decades, there were rapid advances in science related to prenatal screening and diagnosis of foetal Down syndrome. With the arrival of NIPD, it will radically change our obstetric practice. Further developments will certainly enable us to detect more disorders. However, we must be very careful in the early stage of implementation of this new test, so as to avoid unnecessary complications, potential misuse and abuse.

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Prenatal screening and diagnosis of foetal Down syndrome (Trisomy 21)" by Dr. Tze-kin LAU and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 July 2012. 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. **In experienced hands, the procedure-related risks of amniocentesis and chorionic villus sampling are similar.**
2. **First trimester amniocentesis is as safe as second trimester amniocentesis.**
3. **Rapid karyotyping allows the detection of all abnormalities that can be detected by conventional karyotyping.**
4. **Maternal age as a screening test for fetal Down syndrome is highly efficiency with a detection rate of over 60%.**
5. **Sonographic measurement of fetal Nuchal Translucency should be performed only by accredited operators.**
6. **Positive predictive value of a screening test is affected by the detection rate and false positive rate of the test, as well as the prevalence of the condition.**
7. **Fetal DNA is present is detectable amount in the maternal plasma at 12 weeks of gestation in all pregnancies.**
8. **Fetal cell free DNA persists in the maternal plasma months after delivery.**
9. **Non-invasive prenatal test for fetal Down syndrome by maternal plasma DNA sequencing is now a clinical reality with a detection rate of over 99% and a false positive rate of below 1%.**
10. **If the Non-invasive prenatal test for fetal Down syndrome by maternal plasma DNA sequencing is positive, termination of pregnancy is an acceptable management option.**

ANSWER SHEET FOR JULY 2012

Please return the completed answer sheet to the Federation Secretariat on or before 31 July 2012 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Prenatal screening and diagnosis of foetal Down syndrome (Trisomy 21)

Dr. Tze-kin LAU

MBChB (CUHK), MMed (O&G)(Singapore), MD (CUHK), FRCOG (UK), FHKCOG, FHKAM (O&G)

Specialist in Obstetrics and Gynaecology (Private practice)

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Answers to June 2012 Issue

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Fertility Preservation for Cancer Patients

Dr. Ernest HY NG

MD, FRCOG, FHKAM (O&G)

Associate Professor, Department of Obstetrics and Gynaecology, University of Hong Kong

Dr. Ernest HY NG

Introduction

Continued advances in the early diagnosis and treatment have significantly improved the survival of patients suffering from cancers. High dose chemotherapy and / or radiotherapy treatment increase the cure rate in patients of reproductive age and younger but may damage their gonadal tissue resulting in permanent sterility. The germinal epithelium is very sensitive to chemotherapy, especially to the alkylating agents, and effects of irradiation.

Fertility preservation for patients with cancer is becoming a hot topic recently because of reported live births following transplantation of frozen ovarian tissues from cancer patients and the advance in the method for freezing oocytes. This article will summarise the assessment needed for patients requesting fertility preservation, sperm freezing for male patients and various options for female patients.

Assessment

Any oncologist who sees young and reproductive-aged patients for consideration of cancer therapy should address potential treatment-related sterility and discuss the availability of fertility preservation with them or their parents at the earliest possible opportunity. The risk of gonadal toxicity by the cancer therapy and the survival rate should be carefully assessed. If patients express a strong fertility wish, they should be referred to reproductive specialists for further counselling about the options of fertility preservation, taking into consideration their age, marital status and general condition (Figure 1).

Sperm freezing for male patients

Sperm freezing is non-invasive and can be offered by most assisted reproduction treatment centres within a very short time, causing no delay in the cancer treatment. Therefore, guidelines from the National Institute for Health and Clinical Excellence state that any man or adolescent boy should be offered the opportunity to store their sperm if they are receiving treatment that may render them infertile. If time before cancer therapy allows, two to three semen samples produced at least 48 hours apart may be obtained.

The sperm quality markedly deteriorates after a single course of chemotherapy and preservation should be performed prior to initiation[1]. Men with testicular and haematological cancers may present with poor semen parameters prior to commencement of chemotherapy / radiotherapy[2]. Some may not be able to produce semen samples by masturbation because of the poor physical condition and the stress.

In Hong Kong, the maximum period for storing sperm for cancer patients is for 10 years or until the men reach the age of 55, whichever is later. Their stored sperm can be used for insemination or other reproductive technology procedures only after legal marriage. Upon their deaths, their stored sperm cannot be used by their spouses to bring about a posthumous child(ren).

In those men who are found to have no sperm in the ejaculate after chemotherapy, they can be counselled that sperm can still be found in testicular sperm extraction in some patients[3]. Penile vibration and electroejaculation under general anaesthesia have been used to obtain sperm in pubertal boys who are not ready to produce a semen sample. Cryopreservation of testicular tissues in prepubertal boys is still considered experimental at the present time.

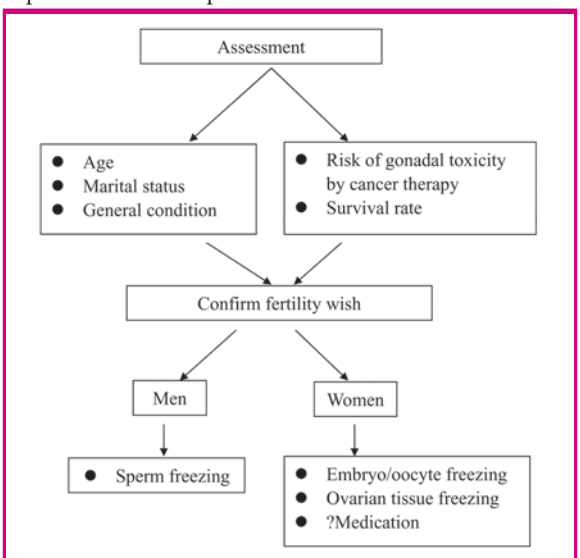

Figure 1: Assessment for fertility preservation

Fertility options in female patients

The options include fertility sparing operation, embryo/

oocyte freezing, ovarian tissue freezing and medication.

1. Fertility sparing operation

Ovarian transposition can be performed when pelvic radiation is used for cancer therapy so that the ovaries can be surgically moved as far as possible from the radiation field through laparotomy or laparoscopy. The overall success rate as determined by the presence of menstrual function is approximately 50% because of scattered radiation and alteration of ovarian blood supply after ovarian transposition. The patient may be able to get pregnant spontaneously, after reposition of the ovaries or in vitro fertilizsation (IVF) treatment.

Fertility sparing operations can also be considered in some well-selected patients with gynaecological malignancy. The majority of patients with ovarian carcinoma present with advanced disease but borderline tumours and FIGO stage I tumours are more common in women of reproductive age. In patients who have borderline tumours of the ovary and a strong fertility wish, surgical management may be limited to unilateral salpingo-oophorectomy with complete surgical staging if the tumour appears confined to one ovary[4]. Similarly, in patients with well-differentiated, encapsulated, unilateral lesions without adhesions and ascites, a unilateral salpingo-oophorectomy and complete staging, with the preservation of contralateral ovary may be considered after comprehensive counselling with the gynaecological oncologist.

Progestin hormonal therapy may be tried first in selected young patients with well differentiated, early endometrial cancer who have a strong fertility wish, rather than total hysterectomy and bilateral oophorectomy[5]. Repeated sampling of the endometrium is required. If persistence or progression is found, hysterectomy is recommended. In cases where regression occurs, continued hormonal therapy for an additional 6-9 months is acceptable. At completion of treatment, in the absence of relapse, the patient is encouraged to pursue pregnancy with the aid of assisted reproduction, which increases the chance of successful conception and also decreases the interval to conception. Patients should be accurately informed about the relatively high recurrence rates even after complete response to the hormonal treatment.

In patients who are under the age of 40 and diagnosed with cervical carcinoma, radical trachelectomy in which the cervix is removed but the uterus is spared can be considered if the disease is stage 1A2-IB with less than 2 cm in diameter and less than 10mm invasion[6]. These patients after radical trachelectomy may experience a higher incidence of subfertility due to cervical abnormalities. There is also an increased risk in mid-trimester losses and preterm births.

2. Embryo and oocyte freezing

Embryo freezing is a well established technique and is widely available in assisted reproduction treatment centres. Women have to undergo ovarian stimulation which may take 10-14 days from the start of the next period. An average of approximately 10 oocytes may be obtained but it depends on the woman's age and her ovarian reserve. Oocytes after the retrieval are fertilised by sperm from their husband. There are no published data showing successful pregnancy rates after IVF carried out as an emergency procedure in patients with cancer but Anderson & Wallace[7] indicated in their experience that success rates may be lower than expected.

A delay of 2-3 weeks for ovarian stimulation may not be acceptable to many patients and their oncologists because this means an inevitable delay in the commencement of cancer therapy which may have an adverse impact on the treatment success. Ovarian stimulation also exposes the woman to supraphysiologically high oestradiol concentrations that may be of importance in a hormone-dependent cancers such as oestrogen receptor positive breast cancer.

Fertilisation of oocyte requires sperm from the husband as in Hong Kong couples must be legally married in Hong Kong to undergo IVF treatment. Oocyte freezing is an alternative possibility for single women. Normally, oocytes will be obtained following ovarian stimulation as for IVF but aspiration of immature oocytes followed by in vitro maturation before freezing has also been described. The success of oocyte freezing using a slow freezing protocol and a vitrification protocol is very low before June 2005 as the corresponding live birth rates per oocyte thawed were 1.9% and 2.0% respectively, as shown in a meta-analysis[8]. However, a more recent randomised trial[9] demonstrated that the ongoing pregnancy rates of using fresh and vitrified oocytes were comparable in an oocyte donation programme, probably as result of refinements in the vitrification method whereby the cell is exposed to a much higher concentration of cryoprotectant than normal for a short period of time only and then cooled very rapidly by direct exposure to liquid nitrogen.

It is at present unclear how many women will return to use embryos or oocytes frozen under these circumstances.

3. Ovarian tissue freezing

Ovarian tissue freezing has the distinct advantage over embryo/oocyte freezing in that no ovarian stimulation is required. That means there is no significant delay in the commencement of cancer therapy. This method can also be used in prepubertal girls and adolescents. However, the ovarian tissue is generally obtained at laparoscopy which can be associated with morbidity. A unilateral oophorectomy or strips of ovarian cortex where most of the primordial follicles lie can be performed.

Proposed guidelines for the selection of adolescent girls and women for ovarian tissue cryopreservation include: age of women <35years, no existing children, good chance of long term survival, significant risk of premature ovarian failure and non previous gonadotoxic chemotherapy[7]. Individualisation is clearly necessary in the actual counselling and provision of this service.

Frozen ovarian tissue after thawing can subsequently be reimplanted orthotopically in the pelvis and a spontaneous pregnancy was reported in 2004[10]. The graft has a certain life span after reimplantation. A significant concern is the possibility of contamination of ovarian tissue by malignant cells which has been confirmed in a murine model. Since the first report in 2004, about 20 women were reported to have children as a result of this method, although it remains unclear how many transplantations of frozen ovarian tissue have been performed globally.

4. Medication

The use of medication to protect the ovary during chemotherapy is an attractive possibility and patients are not required to undergo the invasive procedure for embryo/oocyte freezing and ovarian tissue freezing. Gonadotrophin releasing hormone agonists (GnRHa) are commonly employed for this purpose. The proposed mechanisms by which GnRHa during chemotherapy may decrease follicle depletion are suppression of the pituitary ovarian axis, decreased ovarian perfusion, and a direct gonadal effect that may prevent cellular apoptosis.

In a meta-analysis[11] involving six randomised trials, the incidence of premature ovarian failure or resumption of ovulation both demonstrated a statistically significant difference in favour of the GnRHa co-treatment. However, the occurrence of spontaneous pregnancy showed no statistically significant difference between GnRH cotreatment and the control groups. Many trials did not report pregnancy and used amenorrhoea as the outcome parameter. It is important to stress that the presence of regular cycles and ovulation following chemotherapy does not necessarily indicate that the women can get pregnant. Large randomised trials are now underway in the UK and the United States whose results are eagerly awaited. Patients should be fully counselled before this approach is offered.

Conclusion

Fertility preservation is a rapidly developing field. Sperm cryopreservation is an established treatment for adult men who should be informed of this approach before the commencement of cancer therapy. Female patients should be comprehensively counselled of various options including fertility sparing operations, embryo/oocyte freezing, ovarian tissue freezing and medication.

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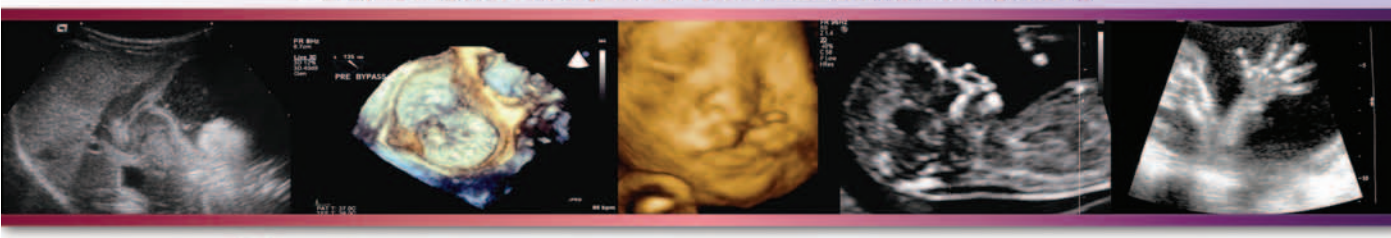

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Real World Experience of Quadrivalent HPV Vaccines – Not Just a Women's Issue

Dr. Kar-fai TAM

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Specialist in Obstetrics and Gynaecology

Dr. Kar-fai TAM

Human Papillomavirus

It is now widely accepted that the Human Papillomavirus (HPV) is the cause for cervical cancers based on the fact that HPV DNA was detected in 99.7% of cervical cancer samples.[1] Human Papillomaviruses are small DNA viruses that infect epithelial tissues. HPV consists of 8,000 base-paired long circular DNA molecules wrapped into a protein shell, which is composed of two molecules including the L1 and L2. More than 100 types of HPVs have now been molecularly characterised and about 40 types are able to infect the genital tract. A subset of mucotrophic high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73 and 82) belonging to the alpha genus is associated with more than 99% of the cervical cancers.1 Among the high-risk HPV types, HPV-16 and -18 accounted for about 70% of all the cervical cancers.[2] Together with another six high-risk HPV types including 31, 33, 35, 45, 52 and 58, they are the eight most common HPV types accounting for about 90% of the cases. However, the relative importance of HPV types 31, 33, 35, 45, 52 and 58 appeared somewhat different among different continents.[3] Based on the knowledge on HPV and its causative effects on cervical cancer, HPV vaccines were developed to prevent this disease.

Other than cervical cancer, HPV can also cause a wide range of diseases including cancer and precancerous changes of the vagina, vulva, penis and anus, as well as genital warts.

Quadrivalent HPV Vaccine

There are now two HPV vaccines in the market for the prevention of cervical cancer. Gardasil® (Merck and Co., Inc.) is the quadrivalent HPV vaccine. It consists of purified L1 VLPs of HPV types 6/11/16/18 at 20/40/40/20μg per dose formulated on 225μg of aluminum adjuvant hydroxyphosphate sulfate. The product is to be delivered by intramuscular injection as a 0.5ml dose at 0, 2 and 6 months.[4]

How Does the Prophylactic Vaccine Work?

Virus like particles (VLPs) containing the L1 capsid protein was created through recombinant DNA technology. This antigen if presented to the immune system would induce the production of neutralising antibodies. The early evidences of protection from HPV infection by antibodies came from animal studies[5,6] The protective effect was believed to be conferred to the IgG, which is present in the epithelium neutralising the virus particles and prevents infection. The VLPs do not contain genetic materials and therefore they are non-infectious and will not cause genital infection. The antibodies induced by the VLPs are type specific and therefore they prevent infection of the relevant viruses only. However, some evidences from recently published data did suggest that there was cross protection against other HPVs of the same phylogenetic subtype, which share the same conformational epitopes.

Indications for the Quadrivalent Vaccine in Hong Kong

The quadrivalent vaccine in Hong Kong is indicated in females from the age of 9 to 45. It is for the prevention of cervical, vaginal and vulval cancers and precancerous changes as well as genital warts. For males, it is indicated from the age of 9 to 26 for the prevention of genital warts.

Areas of Protection

HPV-16 and -18 related diseases: The quadrivalent HPV vaccine, Gardasil® offers protection against cervical cancers through the prevention of HPV-16 and -18 infections and thus cervical intraepithelial neoplasia (CIN) grade 2-3 with an efficacy of about 98%.[7] Gardasil® also offers protection against HPV-16 and -18 related vaginal intraepithelial neoplasia (VAIN) grade 2-3 and vulval intraepithelial neoplasia (VIN) grade 2-3 with an efficacy of 100%.[7] There were two studies conducted to look into the efficacy of quadrivalent HPV vaccine against HPV related diseases in males.[8,9] It was found that the vaccine can effectively reduce the rate of HPV-16 and -18 related anal intraepithelial neoplasia (AIN) grade 2-3 in men who have sex with men. Protection against penile intraepithelial neoplasia was observed in a study, however, the number was too small for any clinical significance.

HPV -6 and -11 related diseases: The quadrivalent HPV vaccine offers protection against genital warts in both males and females, through the prevention of HPV-6 and -11 infections with an efficacy over 90%.[7]

Safety

Details of the safety data were obtained prospectively during the clinical trials.[7] The most commonly reported adverse events were pain, redness or swelling over the injection sites. Fever was also common (one in 10 subjects) but most of these were low grade. No significant increase in serious adverse events was found in the vaccine group when compared to the placebo group. Data on pregnancy including the foetal outcome are now being collected in ongoing studies. So far, no vaccine-related adverse foetal outcome has been evident.

Immunogenicity

Quadrivalent HPV vaccine is highly immunogenic causing seroconversion in more than 98% of subjects.[7] The peak antibody titres were achieved one month after the completion of all the three doses of vaccination and then started to decline. After a follow-up period of 4.5 – 5 years, the antibody titres were still found to be higher than the antibody titres caused by a natural infection.[10] Moreover, protection against HPV infection or HPV related diseases were observed in a wide range of antibody titres.

Duration of Protection

Currently, the duration of protection provided by the quadrivalent HPV vaccine is not known. However, long term follow up of a cohort of subjects in the Nordic countries (unpublished data) have shown that efficacy is maintained for at least seven years. Up to this moment, the necessity for booster injections is still unclear.

Target Population for the HPV Vaccines

To achieve better protection, vaccines have to be delivered before exposure to the viruses. Since HPV is mainly transmitted sexually,[11] the vaccines should be given before sexual exposure. As better immune response was found in pre-pubertal subjects with higher antibody titres, injection before puberty may achieve better results. [11,12]

Gender

Genital warts and AIN do concern both men and women but not cervical, vaginal, vulval cancers or their precancerous lesions. Penile cancers occur in men but with a much lower incidence when compared with cervical caners.[13] From the mathematical models, vaccination for men could further reduce the incidence of cervical cancers.[14] However, the cost-effectiveness is a major concern to most of the policy makers. For those localities having a high prevalence of genital warts, including men in the vaccination programme using the quadrivalent vaccine, which helps preventing 90% of the genital warts, would make it easier to justify. For males having higher risk of AIN, protection against this disease is now an indication for the usage of the quadrivalent HPV vaccine in the United States.

Pregnancy

So far, there is no evidence showing vaccine-related adverse pregnancy outcomes. Nevertheless, those who are pregnant or contemplating pregnancy are advised against vaccination.

HPV Positive Subjects or those Who Had History of Abnormal Cervical Cytology or Cervical Intraepithelial Neoplasia (CIN)

The vaccine, which is now available, is a prophylactic vaccine. A cytotoxic and T-cell response is required to clear up the infected cells and this immune response is probably not triggered by the dose and way the VLPs are administered. It has been believed that individuals who have been infected with the corresponding HPV types would lose the protection to the specific type of HPV from the vaccine. However, a recent publication showed that quadrivalent vaccine injection in subjects who were previously treated for HPV related diseases, could reduce the risk of recurrent HPV related diseases including those high grade precancerous cervical changes.[15] If one has been infected by HPV types of the corresponding vaccines, leading to abnormal cervical cytology or CIN, the protective effect of the vaccines would not be as high as quoted. Using the currently available commercial kit, one cannot tell the causative HPV type leading to the abnormalities. Therefore, a history of CIN or abnormal cytology is not a contraindication for vaccination but one should bear in mind that the efficacy of the vaccines could be diminished. A negative serology test or HPV DNA test is not a reliable test on any prior HPV infection. Therefore, a routine HPV serology test or HPV DNA test is not recommended before the use of vaccines.

Real World Experience after the Implementation of Immunisation Programme

In Australia, the vaccination programme using the quadrivalent HPV vaccine was started in 2007. After the commencement of the immunisation programme, a decrease in the incidence of high grade cervical abnormalities in girls under the age of 18 within 3 years after the implementation of the population-wide HPV vaccination programme was observed.[16] On the other hand, there was also a dramatic drop in the incidence of genital warts in young women and men below the age of 21, four years after the commencement of the immunisation programme.[17]

Cervical Cancer Screening after Vaccination

HPV vaccine does not provide 100% protection from cervical cancers. It is very important to note that whoever receives the vaccine should continue with cervical cytology screening. However, the chance of having abnormal cervical cytology or CIN may be lower when compared to the population without HPV vaccination. In the future, the mode of screening may be changed if the vaccine is incorporated in the immunisation programme. In the meantime, we do not have enough evidence to substantiate a change in our screening policy.

Conclusion

HPV causes a wide range of diseases from genital warts to cancers of the female genital tract and anus, which is a major burden to the health care system especially in the developing countries. The quadrivalent HPV vaccine has been proven effective in the prevention of high grade precancerous lesions of the cervix, vagina and vulva as well as AIN in men who have sex with men. The vaccine is also highly effective in the prevention of genital warts in both men and women. The effect of the vaccine lasts for at least 5 years and so far, there is no recommendation for the need of booster doses.

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The only HPV Vaccine that can protect MALE & FEMALE against MORE HPV-related diseases[1]

Australia:
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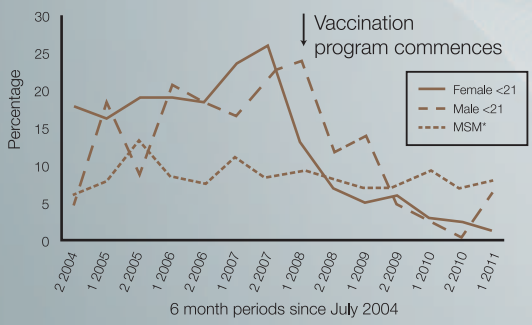
Significant impact on high grade cervical disease and genital warts

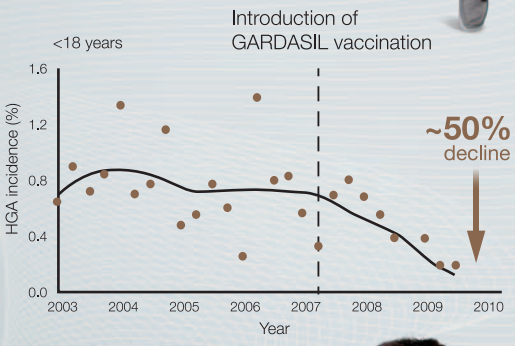
The near disappearance of genital warts in young women 4 years after commencing GARDASIL vaccination programme in Australia[2]

Female <21: ↓ 90% Male <21: ↓ 87%



*MSM=Men who have sex with men
Adapted from Read et al.[2]

First report of a decrease of CIN 2/3 or AIS after commencing GARDASIL vaccination program in Australia[3]



HGA = high-grade cervical abnormalities (cervical intraepithelial neoplasia of grade 2 or worse or adenocarcinoma in situ)
Adapted from Brotherton et al.[3]

UK switches to GARDASIL for national HPV vaccination in Sept 2012 following a competitive tendering exercise[4]

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"GARDASIL is contraindicated in individuals with hypersensitivity to any vaccine ingredients or after a previous dose of GARDASIL. It is not recommended for pregnant women and pregnancy should be avoided during the vaccination period. This vaccine will not protect against diseases that are not caused by HPV and is not intended to be used for treatment of active genital warts; cervical, vulvar, or vaginal cancers; CIN, VIN, or VaIN. Routine cervical screening should be continued. Vaccinees should be carefully observed for approximately 15 minutes after administration of GARDASIL. Common adverse reaction in clinical trials were: headache, dizziness, nausea, pain in extremity, pyrexia, injection site reactions: erythema, pain & swelling; pruritus & hematoma which were mild to moderate. Post-marketing reports: dizziness, headache, syncope, nausea & vomiting, arthralgia, asthenia, lymphadenopathy, urticaria"

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VACC-1023473-0027 05/12

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Updated Consensus Statement on the use of Tibolone in Asian Women (Level of evidence 1b)[1]: Livial® relieves estrogen deficiency symptoms in postmenopausal women[1,2]:

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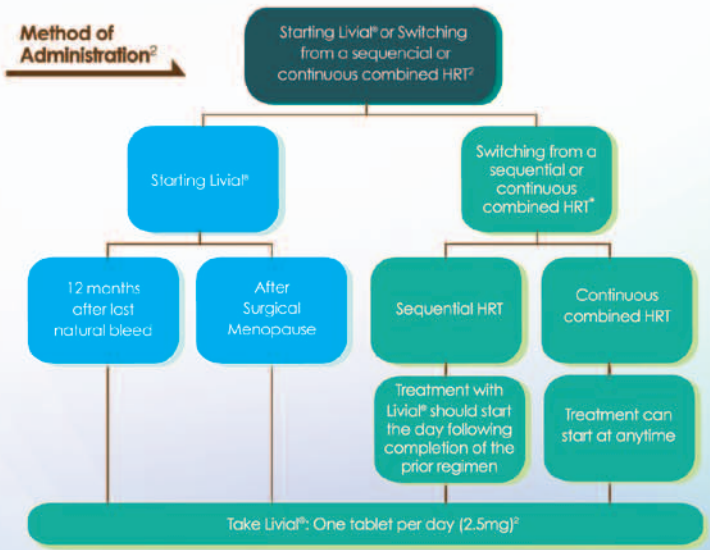

*Any irregular/unscheduled vaginal bleeding, either on or off HRT, for which there is no obvious cause, should be investigated before starting **Livial®** (see **Contraindications**).*

Before prescribing, please consult the full prescribing information.

Selected Safety Information for Livial®:

-Indications: Treatment of estrogen deficiency symptoms in postmenopausal women, more than one year after menopause; prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis. The decision to prescribe tibolone should be based on an assessment of the individual patient's overall risks and, particularly in the over 60s, should include consideration of the risk of stroke.

-Contraindications: Pregnancy and lactation; known, past or suspected breast cancer; known or suspected estrogen-dependent malignan tumors (e.g. endometrial cancer); Undiagnosed genital bleeding; Untreated endometrial hyperplasia; previous idiopathic or current venous thromboembolism (deep venous thrombosis, pulmonary embolism); arterial thromboembolic disease (e.g. angina, myocardial infaction); liver disease (acute or history); Known hypersensitivity to the active substance or to any of the excipients; Porphyria.

-Precautions: Therapy should be discontinued in the following situations: Jaundice or deterioration in liver function; Significant increase in blood pressure; New onset of migraine-type headache. Conditions need supervision:Leiomyoma (uterine fibroids) or endometriosis, A history of, or risk factors for, thromboembolic disorders, Risk factors for estrogen dependent tumors, Hypertension, Liver disorders, Diabetes mellitus with or without vascular involvement, Cholelithiasis, Migraine or (severe) headache, Systemic lupus erythematosis, A history of endometrial hyperplasia, Epilepsy, Asthma and Otosclerosis.

-Common side effects in clinical studies: lower abdominal pain, abnormal hair growth, vaginal discharge, candidiasis or haemorrhage; endometrial wall thickening, postmenopausal haemorrhage, breast tenderness, genital pruritus, pelvic pain, cervical dysplasia, genital discharge, vulvoaginitis, weight increase, abnormal cervical smear.

EPT = Estrogen-Progestogen Therapy

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Emergent Therapeutic Applications of Human Umbilical Cord Mesenchymal Stem Cells

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Introduction

Successful isolation, culture expansion under good manufacturing practices and cryopreservation of human umbilical cord mesenchymal stem cells (hUC-MSC) provide an exceptional opportunity to cure difficult diseases via a restorative approach. Mesenchymal stem cells (MSC) found in various neonatal or adult connective tissues, respond to ischaemia, tissue injury and inflammation with marked proliferation, immunomodulation and migration. The capacities of self-renewal and multi-lineage differentiation into bone, cartilage and adipose tissues contribute to the development of regenerative medicine and cell-based therapy. Systemically administered MSC seem to preferentially migrate to the site of injury, where they support functional recovery. Apart from differentiation into mesodermal tissue for tissue repair, there is evidence of transdifferentiation into ectodermal and endodermal tissues, thus expanding the scope in clinical trials of various medical conditions. MSC are characterised by being plastic adherent in culture setting, as spindle-shaped fibroblastoid cells. They could serve as feeder layers in cell cultures of haematopoietic stem cells. Despite the heterogeneity, MSC express cell markers CD73, CD90, and CD105, while negative for haematopoietic cell markers CD34, CD45, HLA-DR. Neonatal tissues, such as human umbilical cord is a readily available supply of MSC, with high potential in culture expansion in vitro for therapeutic applications. The rapid availability, absence of donor risks, with lower risk of transmissible infectious diseases are favourable factors for cryopreservation of hUC-MSC for future clinical applications.

MSC Treatment

MSC transplantation, either allogeneic or autologous, could result in therapeutic efficacy, low rejection, low immune reactivity, and without teratogenic transformation. In contrast with haematopoietic stem cell transplant, intensive myeloablative preconditioning treatment and HLA typing is not required, thus allowing timely treatment even in patients with urgent medical problems. Various means of infusion of ex-vivo expanded MSC suspension, intravenous, local injection, intrathecal, are well tolerated with minimal side effects in a number of clinical trials. By regenerating tissues and immunomodulation, clinical trials using MSC in various therapeutic areas have been developed, including (a) haematopoietic stem cells transplantation by promoting engraftment of donor blood cells; (b) stroke, neurodegenerative disorders (Parkinson's disease, Alzheimer's disease), neurodevelopmental disorders (cerebral palsy, autism), due to the release of trophic factors and induction of neurogenesis; (c) demyelinating conditions (multiple sclerosis) due to inhibition of production of myelin-specific antibodies and encephalitogenic T cells as well as decreased axonal loss; (d) myocardial infarct due to generation of cardiomyocytes and vascular structures and decrease the restenosis rate; (e) type 1 diabetes due to endogenous repair of pancreatic islets and inhibition of the proliferation of β-cell-specific T cells; (f) resistant autoimmune conditions and graft versus host disease, due to inhibition of T cell proliferation and suppressed production of pro-inflammatory cytokines as well as induction of regulatory T cells; (g) liver failure due to inhibition of leucocyte invasion; (h) renal failure due to tubular regeneration through IGF-1 secretion; (i) acute lung injury due to inhibition of proinflammatory cytokine and increased secretion of IL-10; (j) skin grafting due to prolonging skin graft survival; (k) solid organ transplant due to lower rejection risks from immunomodulation and tolerance induction; (l) bone and cartilage regeneration as in osteogenesis imperfecta; (m) bladder reconstruction; (n) peripheral artery disease; (o) retinal degeneration due to anti-apoptotic properties; (p) inner ear damage; (q) gene therapy; (r) HIV treatment; (s) cell-based immunotherapy for cancer; (t) biomaterial engineering etc. The clinical effectiveness of MSC treatment, however, would take some time to confirm with phase III clinical trials. It is apparent that MSC from different sources and in different culture settings differ dramatically in their properties and probably in their therapeutic potential. Thus, deeper understanding in the mechanism of action would allow us to apply the treatment in the most sensible manner.

Immunoregulatory Activities of MSC

One of the most intriguing features of MSC is that they can escape immune recognition of the host as well as inhibit both innate and adaptive immune responses. The immunomodulatory effects on T cells, B cells, natural killer cells, and dendritic cells play an important role in the management of various immune related conditions such as post-transplant graft-versus-host disease (GVHD). MSC impair immune cell proliferation either through, cell- cell interaction, or secretion of cytokines, or a combination of both. It inhibits the innate immunity by suppressing dendritic cell maturation, impairing the antigen presenting function, and downregulation of proinflammatory signals. In addition, MSC impair

the cytotoxic activities of natural killer cells as well as neutrophils. The adaptive immunity is regulated by the suppression of T cell proliferation by MSC, such as antigen specific CD8+ cytotoxic T lymphocytes, antigen specific antibody production by B lymphocytes. On the other hand, MSC induce the proliferation of T regulatory cells, resulting in homeostasis and tolerance of self- antigens.

Role in Haematopoietic Stem Cell Transplant

MSC bring refractory GVHD under control without impairing T cell immunity against viral infections. It has been shown that the therapeutic efficacy of unrelated MSC sources is comparable to HLA-identical or haploidentical sources, supporting banking of cryopreserved cells for immediate accessibility of MSC treatment. The MSC infusion is in general well tolerated without significant clinical events. Initial clinical studies in the prophylaxis of GVHD appear promising as well. Besides, hUC-MSC has been shown to facilitate engraftment of donor blood cells in transplant settings, either enhancing engraftment or treating graft failure. It is likely due to cytokine production of MSC supporting the recovery of marrow function. Transplanting transfusion dependent thalassaemia without HLA identical siblings faces significant engraftment problems and GVHD. Haematopoietic stem cells and MSC cotransplantation is being studied to target these issues with reduced intensity pre-transplant conditioning regimes.

Role in Central Nervous System Conditions

There is ample evidence that mesenchymal stem cells derived from umbilical cords could trans-differentiate into neural cells both in vitro and in vivo. Cord stem cells could be induced to express neuronal, astrocytic and oligodendroglial markers in the presence of specific neuronal condition medium experimentally. Up regulation of transcription factors involved in early neurogenesis could also be induced. Transplantation in animal models demonstrate biological benefits in reducing motor deficit in Parkinson disease and ischaemic brain damage. MSC can rescue neurons and oligodendrocytes from apoptosis through the release of trophic and anti-apoptotic molecules, and they can have anti-inflammatory and anti-proliferative effects on microglial cells and astrocytes, resulting in the induction of a neuroprotective microenvironment. In addition, MSC can promote the proliferation and maturation of local neural precursor cells, leading to their differentiation into neurons and oligodendrocytes. Both direct intra-parenchymal injection into brain lesions and intravenous infusion of cord stem cells have been shown to minimise the extent of brain tissue loss and handicap in animal models of stroke and spinal cord injury. Apparently, it seems that engraftment of stem cells into the diseased area is not always necessary to produce the treatment effects, though stem cells could be found throughout the brain parenchyma and spinal cord expressing neural and glial markers. Another mechanism could be that stem cells may induce neuro-protective factors to minimise the damage and hasten recovery in a local manner. MSC treatment could promote regeneration and growth of axons across the damaged site in complete spinal cord injury, by providing growth factors and opposing growth inhibitors. MSC would migrate into the lesional area and form a continuous bridge for axonal repair during recovery.

Role in Cardiovascular Conditions

In order to restore diseased heart, hUC-MSC could be transformed into cardiomyocytes, rebuilding the myocardium as well as into the endothelial cell, building the vascular network. The repopulation of functional cardiomyocytes over the infarcted area would minimise scar tissue formation, and hence lowering the risk of development of cardiac failure. The cytokine secretion would improve tissue perfusion, promoting angiogenesis, recruiting progenitor cells, decreasing apoptosis, with less collagen deposition and fibrosis. Apart from acute ischaemic damages, subacute and chronic ischaemic animal models confirm the role of MSC in various cardiac conditions. Clinical studies involving allogeneic MSC would be more useful clinically as the administration of cell treatment could be performed in a more timely manner.

Conclusion

Registered clinical trials involving MSC are ever increasing, currently more than two hundred of them. Current evidences suggest that MSC transplants are safe without malignancy risks. MSC transplantation trials recruit both autologous and allogeneic cells and employ both freshly-isolated and ex-vivo culture expanded cell populations. Properly designed clinical trials, based on basic science from the laboratory bench, with multi-disciplinary scientists and clinicians, will soon provide us with new treatment options in difficult diseases. Processing and storage of MSC from umbilical cord will certainly provide us with a large pool of readily available source of stem cells for future clinical therapeutics. Thus far, the application of hUC-MSC depends on a consistent definition of the MSC production, with stringent manufacturing standard and safety measures. The timing of MSC infusions, cell doses, and delivery methods and the MSC engraftment would need consensus as well as clarification with more basic science data. Further understanding of the cellular mechanism, cytokine production, and cell distribution status would promote the MSC therapy.

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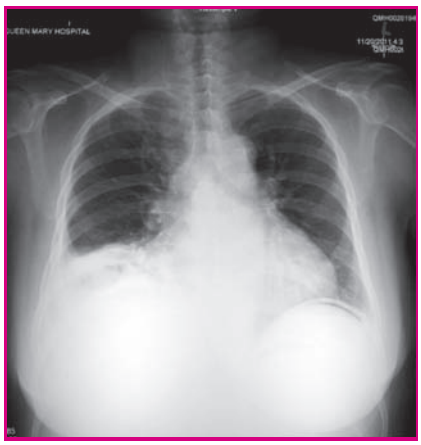
Radiology Quiz

Dr. KY CHO

Department of Radiology, Queen Mary Hospital



History:

53 year-old female.
Complained of acute epigastric pain.

Imaging:

Plain radiograph of the chest (PA erect)

Question:

What are the imaging findings and diagnosis?

(See P.33 for answers)

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Association for Integrative Aesthetic Medicine, Hong Kong (AIAM)
香港中西醫美容醫學學會

Association for Integrative Aesthetic Medicine, Hong Kong (AIAM) has been established for almost 4 years since July, 2008. It was set up by a group of specialists in both Western & Chinese Medicine, having ideals in putting the proficiency and expertise knowledge of the members in both Western & Chinese Medicine into the development of Aesthetic Medicine.

The objectives of the Association are:

- Advancements of academic activities be put as the first priority;
- Promotion of useful medical areas from the integration of Western & Chinese Medicine;
- Contribution to Aesthetic Medicine in medical science, technology and skills.

The Association at present consists of a Council with the following members:

President :	Dr & CMP Yu Chau Leung Edwin 西醫及中醫師余秋良 (Vice President of the Hong Kong Association for Integration of Chinese-Western Medicine)
Vice President :	Dr Daniel Lee Tin Chak 李天澤醫生 (Specialist in Plastic Surgery)
Vice president :	Dr Hau Ka Lam 侯嘉林醫生 (Specialist in Dermatology)
Vice president :	CMP Huang Fei Li 黃霏莉中醫師 (Hong Kong Baptist University)
Hon. Secretary :	CMP Fu Wen Shu 符文澍中醫師 (Hong Kong Chinese University)
Hon. Treasury :	Dr Chan Kam Tim Michael 陳錦添醫生 (Specialist in Dermatology)
Council members :	Dr Chow Wing Cheong Louis 周永昌醫生 Dr Hui Edward 許嘉榮醫生 CMP Yeung Ming Ha, Jenny 楊明霞中醫師
Hon. Advisor :	Prof. Lau W.Y.Joseph 劉允怡教授
Hon. Research Consultant :	Prof. Leung Ping Chung 梁秉中教授

The Hong Kong Society for Histocompatibility and Immunogenetics

The Hong Kong Society for Histocompatibility and Immunogenetics (HKSHI) was incorporated as a limited liability company on 8 July, 2011. The primary objectives of the Society are to contribute to the advancement of science, education and application in histocompatibility and immunogenetics; to advocate the international standards of laboratory testing in histocompatibility and Immunogenetics in the interest of optimal patient care; to provide a forum for the exchange of knowledge and information of histocompatibility and immunogenetics and to strengthen the co-operation, communication, exchange of ideas and opinion between the local and overseas professionals in histocompatibility and immunogenetics.

The major activities include organisation of scientific meetings, seminars and workshops and sponsoring individual members for course registration/ conference/ workshop. There are four classes of membership open for application. They include Fellow Members, Associate Members, Company Members and Overseas Members. The existing members include medical practitioner, nurses, scientist and laboratory personnel etc. Further detailed information and application forms can be accessed at http://www.hkshi.org.

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Part-time Postgraduate Courses

www.fmpg.hku.hk

Department of Family Medicine and Primary Care
The University of Hong Kong

Postgraduate Diploma in Community Geriatrics
社區老年醫學深造文憑

Admission is now open for **practicing doctors** as well as **L.M.C. candidates.**
Students can also attain the Diploma in Geriatric Medicine (DGM) offered by the Royal College of Physicians and Surgeons of Glasgow.

Distance Learning	10 weeks + 6 short assignments
Interactive Workshops	Sept 8, 22, Oct 13, 27, Nov 17 (Saturdays 2:30-5:15 pm)
Clinical Attachment Nov 2012 – May 2013	25 weekday afternoons (2:00-4:00 pm) or weekday evenings (6:30-8:30 pm)

Postgraduate Diploma in Community Psychological Medicine
社區精神醫學深造文憑

Celebrating its 10th Anniversary, this course has been training doctors to treat patients with common psychological problems, such as mood, somatoform, panic, sleep disorders etc.

Interactive Seminars	20 Saturday afternoons between Sept 2012 – Jan 2013
Clinical Attachment	20 weekday afternoons between Jan – June 2013

Quotable Qualification by the Medical Council of Hong Kong

Tuition fee of each course is **HK$42,000** (subject to adjustment)
Online application: **www.asa.hku.hk/admissions/tpg/**
Closing Date for Application: **31 July 2012**

Certificate Course in Clinical Dermatology
臨床皮膚醫學證書課程

Dates: October 6 – December 8, 2012 (10 seminars, every Saturday afternoon)
Time: 2:30 – 4:30 pm (light lunch provided)
Venue: Hong Kong Medical Association Club House, 2/F, 21-22 Connaught Road Central
Tuition fee: HK$ 5,000 (full course); HK$ 700 (per seminar)

Enrolment is now open for **doctors, healthcare professionals** as well as **L.M.C. candidates.**

Closing Date for Application: **3 September 2012**

Telephone: 2518 5681 Fax: 2814 7475 Email: fmpg@hku.hk
Address: 3/F, Ap Lei Chau Clinic, 161 Main Street, Ap Lei Chau, Hong Kong

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
1	* 2012 Hong Kong International Dragon Boat Races 2	* New Update for Hypertension and Atrial Fibrillation * FMSHK Officers' Meeting * HKMA Council Meeting 3	4	5	* Joint Surgical Symposium - Recent Advances of Plastic and Reconstructive Surgery on the Face * HKMA Shatin Doctors Network - New Directions in Managing Type 2 Diabetic Patients 6	* Chinese Medicine in Geriatrics, Hong Kong International Integrative Medicine Conference 7
* Chinese Medicine in Geriatrics, Hong Kong International Integrative Medicine Conference * Joint Professional Basketball Tournament 2012 8	9	* HKMA Kln West Community Network– A New Insight in Anticoagulation Therapy - Role of Direct Factor Xa Inhibitor * HKMA-Tai Po Community Network– Understanding and Treatment of Neuropathic Pain 10	* Hong Kong Neurosurgical Society Monthly Academic Meeting –ICP management in traumatic brain injury 11	* HKMA Hong Kong East Community Network –The Placement of DPP-4 Inhibitors * HKMA NTW Community Network – Recent Advance in Treatment of Varicose Veins & Peripheral Arterial Disease * HKMA Kowloon City Community Network – Tips in the Management of Androgenetic Alopecia * HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2012 – Acute kidney failure 12	* HKMA Yau Tsim Mong Community Network – Update in Psoriasis Management 13	* Paediatric Immunology & Infectious Diseases 14
* 11th Hong Kong Dragon Boat Short Course Races 15	16	* HKMA CME – Primary Prevention of Cervical Cancer * HKMA Annual General Meeting 17	* HKMA Yau Tsim Mong Community Network – Clinical Nephrology Update 2012 (Session 1) 18	* HKMA CME – Certificate Course for GPs 2012 * Respiratory Clinical Meeting – A difficult TB case & The Bottleneck * FMSHK Executive Committee Meeting 19	* HKMA Shatin Doctors Network – Toward Maximizing Bronchodilation in COPD 20	21
* Joint Professional Basketball Tournament 2012 (Semi-final) * Annual Charity Concert 22	23	* HKMA Kowloon West Community Network - Gender Neutral HPV Vaccine-The Real World Impact 24	* HKMA CW&S Community Network - Treatment Options for Anxiety Disorder 25	* HKMA Hong Kong East Community Network – Maximizing Bronchodilation in COPD * FMSHK Foundation Committee Meeting 26	* HKMA Shatin Doctors Network – BPH Management - Not Only Focus on Prostate? 27	* HKMA YTM Community Network – Certificate Course on Bringing Better Health to Our Community (3rd Session) 28
29	30	31				

Date / Time	Function	Enquiry / Remarks
2 MON	**2012 Hong Kong International Dragon Boat Races** Organiser: The Hong Kong Medical Association, Venue: Victoria Harbour, East Tsim Sha Tsui	Ms. Dorothy KWOK Tel: 2527 8285
3 TUE 1:00 pm	**New Update for Hypertension and Atrial Fibrillation** Organiser: HKMA-Tai Po Community Network, Speaker: Dr. Lai Wai Keung, Venue: Chiu Chow Garden, Shops 001-003, 1/F, Uptown Plaza, Tai Po, NT	Ms. Iris Poon Tel: 2881 4236 1 CPD point
8:00 pm	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
8:00 pm	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHOI Kin, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Christine WONG Tel: 2527 8285
6 FRI 8:00 am	**Joint Surgical Symposium - Recent Advances of Plastic and Reconstructive Surgery on the Face** Organisers: Department of Surgery The University of Hong Kong & Hong Kong Sanatorium & Hospital, Venue: Hong Kong Academy of Medicine, Chairman: Dr. Chan Yu-Wai, Speakers: Dr. Chung Hon-Ping & Dr. Liu Hin-Lun, Venue: Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 1 CME point
1:00 pm	**HKMA Shatin Doctors Network - New Directions in Managing Type 2 Diabetic Patients** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. CHAN Wing Bun, Venue: Jasmine Room, Level 2, Royal Park Hotel, Shatin, Hong Kong	Miss Candice TONG Tel: 2527 8285
7 SAT *(8)*	**Chinese Medicine in Geriatrics, Hong Kong International Integrative Medicine Conference** Organisers: Hospital Authority & Hong Kong Association for Integration of Chinese-Western Medicine (HKAIM), Venue: Hong Kong Academy of Medicine	Ms Toki CHAN Ms Justin NG Tel: 2871 8787/ 2871 8896
8 SUN 2:00 pm	**Joint Professional Basketball Tournament 2012** Organiser: The Hong Kong Medical Association	Ms. Dorothy KWOK Tel: 2527 8285
10 TUE 1:00 pm	**HKMA Kln West Community Network– A New Insight in Anticoagulation Therapy - Role of Direct Factor Xa Inhibitor** Organiser: HKMA Kln West Community Network, Chairman: Dr. CHAN Ching Pong, Speaker: Dr. LI Siu Lung, Steven, Venue: Crystal Room I-III, 30/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Miss Candice TONG Tel: 2527 8285 1 CPD point
1:45 pm	**HKMA-Tai Po Community Network– Understanding and Treatment of Neuropathic Pain** Organiser: HKMA-Tai Po Community Network, Speaker: Dr. Ip Kai Yuen, Venue: 大埔新達廣場1樓001-003號	Mr. Roget Law Tel: 6622 6966 1 CPD point
11 WED 7:30am	**Hong Kong Neurosurgical Society Monthly Academic Meeting –ICP management in traumatic brain injury** Organiser: Hong Kong Neurosurgical Society, Chairman: Prof POON Wai Sang, Speaker: Dr. CHAN Kit Ying, Venue: Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital	Dr. Gilberto LEUNG Tel: 2255 3368 1.5 CME points
12 THU 1:00 pm	**HKMA Hong Kong East Community Network –The Placement of DPP-4 Inhibitors** Organiser: HKMA Hong Kong East Community Network, Speaker: Dr. MA Pui Shan, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Miss Candice TONG Tel: 2527 8285
1:00 pm	**HKMA NTW Community Network – Recent Advance in Treatment of Varicose Veins & Peripheral Arterial Disease** Organiser: HKMA NTW Community Network, Speaker: Dr. Tse Cheuk Wa, Chad, Venue: Plentiful Delight Banquet, Yuen Long	Mr. Alan LAW Tel: 25278285 1 CPD point
1:00 pm	**HKMA Kowloon City Community Network – Tips in the Management of Androgenetic Alopecia** Organiser: HKMA Kowloon City Community Network, Speaker: Dr. HO Ka Keung, Venue: Sportful Garden Restaurant, 2/F, Site 6, Whampoa Garden, 10 Shung King Street, Hung Hom	Miss Candice TONG Tel: 2527 8285 1 CPD point
2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2012 – Acute kidney failure** Organiser: The Hong Kong Medical Association, Speaker: Dr. Lai Kar Neng, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central	HKMA CME Department Tel: 2527 8452 1 CPD point
13 FRI 1:00 pm	**HKMA Yau Tsim Mong Community Network – Update in Psoriasis Management** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. LAM Tzit Yuen, David, Speaker: Dr. HO Man Hon, Venue: Jade Ballroom, Level 2, Eaton Smart, Hong Kong380 Nathan Road, Kowloon	Miss Candice TONG Tel: 2527 8285
14 SAT 2:00 pm	**Paediatric Immunology & Infectious Diseases** Organiser: Hong Kong College of Paediatricians, Chairmen: Dr. Sik-nin WONG & Dr. Chi-wai LEUNG, Speakers: Prof. Yu-lung LAU, Prof. Ting-fan LEUNG & Prof. Andrew CANT, Venue: M-Ground Lecture, Queen Elizabeth Hospital	Ms. Vanessa WONG Tel: 2871 8773 3 CME points (Category A)
15 SUN 9:00 am	**11th Hong Kong Dragon Boat Short Course Races** Organiser: The Hong Kong Medical Association, Venue: Stanley Main Beach	Ms. Dorothy KWOK Tel: 2527 8285
17 TUE 7:30 pm	**HKMA CME – Primary Prevention of Cervical Cancer** Organiser: The Hong Kong Medical Association, Speaker: Dr. TAM Kar Fai, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	HKMA CME Department Tel: 2527 8452 1 CPD point
9:00 pm	**HKMA Annual General Meeting** Organiser: The Hong Kong Medical Association, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Christine WONG Tel: 2527 8285

Date / Time	Function	Enquiry / Remarks
18 WED 1:00 pm	**HKMA Yau Tsim Mong Community Network – Clinical Nephrology Update 2012 (Session 1)** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. HO Chung Ping, MH, JP, Speaker: Dr. SIU Yui Pong, Gordon; Dr. YUNG Chee Unn, Jonathan, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong	Miss Candice TONG Tel: 2527 8285
19 THU 1:00 pm	**HKMA CME – Certificate Course for GPs 2012** Organiser: The Hong Kong Medical Association, Chairman: Dr. Danny Ma Ping Kwan, Speaker: Dr. Vincent Leung King Sun, Venue: TKO	Ms. Gary Wong Tel: 3513 4821 1 CPD point
6:30 pm	**Respiratory Clinical Meeting – A difficult TB case & The Bottleneck** Organiser: Hong Kong Thoracic Society & American College of Chest Physicians (HK & Macau Chapter), Chairmen: Dr. Chi-chiu LEUNG & Hoi-yee KWAN, Speakers: Dr. Kwok-Chiu CHANG & Dr. Wing-yan CHU, Venue: LG1, Lecture Room, Ruttonjee Hospital	Dr. Fanny WS KO Dr. Arthur CW LAU Tel: 2632 2785 1.5 CME points (HKCP, CSHK) 2 CME points (HKCFP)
8:00 pm	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
20 FRI 1:00 pm	**HKMA Shatin Doctors Network – Toward Maximizing Bronchodilation in COPD** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. CHAN Ka Wing, Joseph, Venue: Jasmine Room, Level 2, Royal Park Hotel, Shatin, Hong Kong	Miss Candice TONG Tel: 2527 8285 1 CPD point
22 SUN 2:00 pm	**Joint Professional Basketball Tournament 2012 (Semi-final)** Organiser: The Hong Kong Medical Association	Ms. Dorothy KWOK Tel: 2527 8285
8:00 pm	**Annual Charity Concert** Organiser: The Hong Kong Medical Association Charitable Foundation, Venue: AC Hall, Hong Kong Baptist University	Ms. Candy YUEN Tel: 2527 8285
24 TUE 1:00 pm	**HKMA Kowloon West Community Network - Gender Neutral HPV Vaccine-The Real World Impact** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. LAM Ngam, Raymond, Speaker: Dr. SIU Shing Shun, Nelson, Venue: Crystal Room I-III, 30/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Miss Candice TONG Tel: 2527 8285
25 WED 1:00 pm	**HKMA CW&S Community Network - Treatment Options for Anxiety Disorder** Organiser: HKMA CW&S Community Network, Chairman: Dr. HO Lai Ching, Sabrina, Speaker: Dr. LAM Mei Ling, May, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central	Mr. Alan LAW Tel: 25278285
26 THU 1:00 pm	**HKMA Hong Kong East Community Network – Maximizing Bronchodilation in COPD** Organiser: HKMA Hong Kong East Community Network, Chairman: Dr. AU Chi Lap, Speaker: Dr. LAW Tse Sam, Grace, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Miss Candice TONG Tel: 2527 8285 1 CPD point
8:00 pm	**FMSHK Foundation Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
27 FRI 1:15 pm	**HKMA Shatin Doctors Network – BPH Management - Not Only Focus on Prostate?** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. CHAN Chi Kwok, Venue: Star Seafood Floating Restaurant, Shatin (2/F., 55-57 Tai Chung Kiu Road, Shatin, NT)	Miss Candice TONG Tel: 2527 8285 1 CPD point
28 SAT 1:00 pm	**HKMA YTM Community Network – Certificate Course on Bringing Better Health to Our Community (3rd Session)** Organiser: YTM Community Network, Speaker: Dr. NG Chun Kong; Dr. LAM Chun, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital,30 Gascoigne Road, Kowloon, Hong Kong	Miss Candice TONG Tel: 2527 8285

CERTIFICATE COURSE FOR NURSES AND ALLIED HEALTH PROFESSIONALS

• Course No. C198 • CME / CNE Course

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Respiratory Medicine 2012

Jointly organised by

The Federation of Medical Societies of Hong Kong

Hong Kong Thoracic Society 香港胸肺學會

美國胸肺學院（港澳分會）

Objectives: The course aims to enlighten the audience on the state-of-the-art and practical issues in some of the most important respiratory conditions.

Date	Topics	Speakers
12 Sep	An update on COPD classification and treatment strategies	Dr. Kam-cheung WONG 黃錦祥醫生 Senior Medical Officer, TB & Chest Wong Tai Sin Hospital
19 Sep	Pneumothorax – clinical features, pathophysiology and management	Dr. Johnny Wai-man CHAN 陳偉文醫生 Consultant, Department of Medicine Queen Elizabeth Hospital
26 Sep	Principles and practice of oxygen therapy in respiratory diseases	Dr. Arthur Chun-wing LAU 劉俊穎醫生 Associate Consultant, ICU Pamela Youde Nethersole Eastern Hospital
3 Oct	Fundamentals in asthma investigations and treatment	Dr. Fanny Wai-san KO 古惠珊醫生 Associate Consultant, Department of Medicine and Therapeutics Prince of Wales Hospital
10 Oct	Investigations and management of Multidrug-resistant TB (MDR-TB) and Extensively drug-resistant TB (XDR-TB)	Dr. Wing-sze LAW 羅穎思醫生 Senior Medical Officer, TB & Chest Department of Health
17 Oct	Cardio-pulmonary exercise testings – clinical practice and research application	Dr. Wai-kei LAM 林偉奇醫生 Associate Consultant, Department of Medicine North District Hospital

Date : 12 September – 17 October 2012 (Every Wednesday)
Time : 7:00 p.m. – 8:30 p.m.
Venue : Lecture Hall, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$750 (6 sessions)
Certificate : Awarded to participants with a minimum attendance of 70%
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

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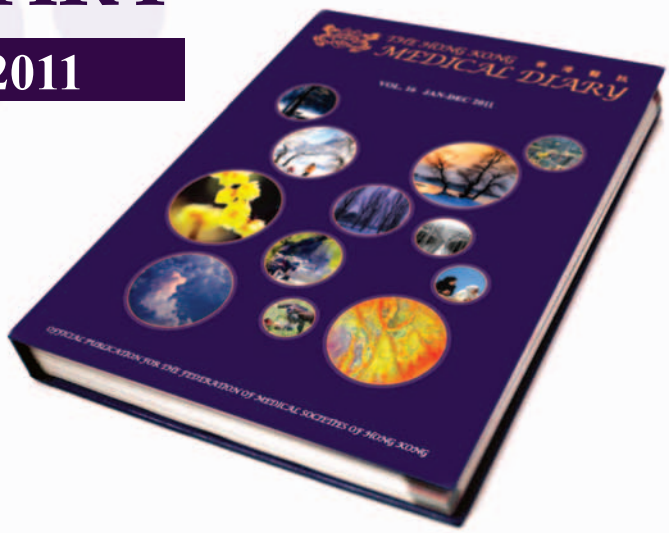
香港醫訊

THE HONG KONG MEDICAL DIARY

VOL. 16 JAN-DEC 2011



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Answer to Radiology Quiz

Imaging findings:

Pneumoperitoneum as suggested by free extra-luminal gas under the left hemidiaphragm.
Mottled gas density at the right subdiaphragmatic region. Air-fluid level is evident.
The right hemidiaphragmatic outline is indistinct and probably elevated.

Diagnosis:

Pneumoperitoneum secondary to ruptured gas-containing liver abscess.

Discussion:

Pneumoperitoneum is gas within the peritoneal cavity, and often is the harbinger of a critical illness.
The most common cause of a pneumoperitoneum is from the disruption of the wall of a hollow viscus.
Many other causes exist however: (abdominal operations, peritoneal dialysis, mechanical ventilation, pneumomediastinum, pneumothorax).
This case illustrates a rare cause of pneumoperitoneum. The mottled gas density with air-fluid level at the right subdiaphragmatic region is actually a large gas-containing liver abscess. The abscess wall ruptured and released gas into the peritoneal cavity. Subsequent contrast CT scan of the abdomen confirmed the diagnosis. It is important to recognise the abnormality in the CXR to make the correct diagnosis and subsequent management.

Dr KY CHO
Department of Radiology, Queen Mary Hospital

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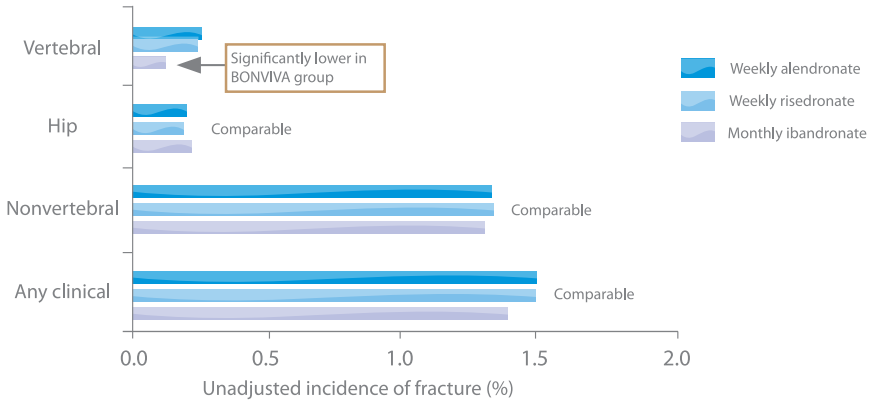
One year retrospective observational fracture study[1]



Bonviva-treated patients had statistically lower incidence of vertebral fractures.[1]

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66%
significant lower risk vs. Alendronate (p=0.004)

BONVIVA
61%
significant lower risk vs. Risedronate (p=0.014)

*The eValuation of IBandronate Efficacy (VIBE) study was a retrospective claims database study with a 12-month observational period that included women ≥45 years of age (n=64,182), newly prescribed monthly oral ibandronate (Bonviva) (n=7345) or weekly oral BPs (alendronate 35 mg or 70 mg, or risedronate 35 mg) (56,837) for a period between April 1, 2005 and December 31, 2005. Ref:1. Bone. 2009;44:758–765. Full prescribing information available upon request

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