TAN TOCK SENG HOSPITAL

MEDICAL DIGEST

APRIL - JUNE 2019

Tan Tock Seng
HOSPITAL

11 Jalan Tan Tock Seng
Singapore 308433

Tel: 6256 6011
Fax: 6252 7282

www.ttsh.com.sg

Medical Digest is a quarterly publication of Tan Tock Seng Hospital written by healthcare providers for healthcare providers, as a service to the medical community.

Tan Tock Seng
HOSPITAL

MCI (P) 126/09/2018

FROM THE EDITOR

For doctors who are self-employed, the objective of their work is evident. For doctors toiling in groups or organisations, the direction and purpose of their work need some consideration.

All organisations publish their vision and mission statements. I think that doctors should take their bearing from these important pronouncements. For example, TTSH's vision is 'Adding years of healthy life' and mission is 'Building on our tradition, Reaching out to the community, Doing our best to serve, care and heal, Together, we aim for excellence in cost-effective healthcare, education and research'.

The Singapore Medical Council's Handbook on Medical Ethics, 2016 edition, does not specifically talk about working in organisations except in the areas of working in a team, and advertising information issued by the doctor's organisation. I quote from page 22: 'If you are working in structured or formal teams (for example, in public healthcare institutions or structured teams in the private sector), you have a responsibility to do what you can to improve the team's performance, correct deficiencies and improve quality of care.' The whole section heavily stresses good patient care.

Dr David Mechanic wrote that doctors who do right build the organisation and, institutes of good repute reciprocally confer gains to her doctors (BMJ 2004; 329: 1418-9). 'Doctors are the gateway to organisational trust. Health plans in the United States elicit trust through the qualifications and reputations of affiliated doctors … In instances where the organisation is held in high public regard … affiliated doctors may also gain in reputation. Doctors and managers stand to benefit by collaborating in building trust in clinicians and in larger systems'.

Our immediate superiors may issue orders that conflict with the published mission. We do not need to agonise because the right path is obvious. We have argued that doctors must remain true to the mission and vision of their institutions, and emphasize good patient care. We cannot go wrong if we hearken to these higher loyalties. Every organisational action must be examined against our values and our interests. Our values must prevail over our interests every time. If we can do good and make a profit, it is fine. If we lose financially when standing by our values, let it be so.

We may not hold high office. We may be torn in different directions. We may be overwhelmed with seemingly purposeless work. We just do our best for our patients and for our organisation. Good must surely follow.

Dr Leong Khai Pang
EDITOR
Medical Digest

We value your feedback. Please email your questions, comments or suggestions to:
ttsh_ccs@ttsh.com.sg
Please also contact us for notification of change of postal address or requests for additional copies.

Prevalence of and risk factors associated with latent tuberculosis in Singapore: A cross-sectional survey

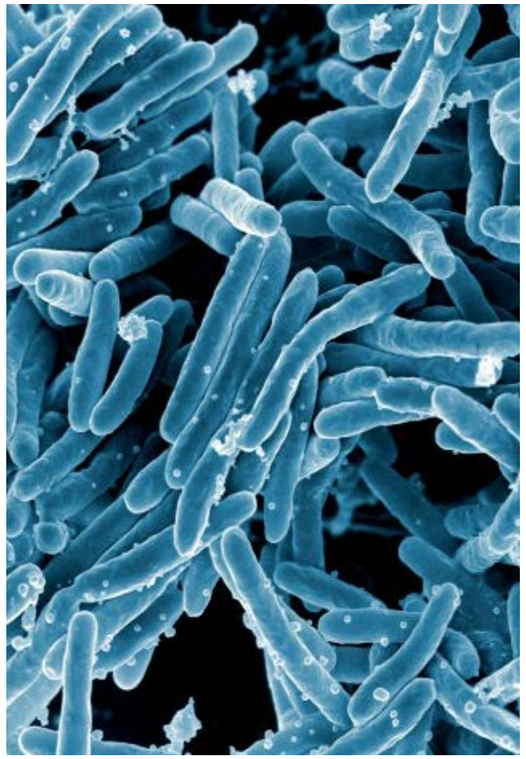
Yap P, Tan KHX, Lim WY, Barkham T, Tan LWL, Chen MI, Wang YT, Chee CBE. Int J Infect Dis. 2018;72:55–62.

IMPORTANCE IN CLINICAL PRACTICE

Information on the background prevalence of LTBI in Singapore residents from this study provides evidence-based guidance to the Singapore TB Elimination Programme (STEP). Contact screening, which is used to identify recently infected contacts at high risk for progression to active disease (and therefore, are candidates for preventive therapy), is carried out according to concentric circles of exposure to the index case starting with the innermost circle. The decision to expand screening is based on the attack rate of each circle and generally, no further expansion of screening is required when the attack rate approaches the background LTBI rate of the community. Knowledge of the age-stratified LTBI prevalence in the community is thus useful in guiding contact investigations. Finally, given the high prevalence of LTBI among foreign-born residents from regional countries, similar studies should also be conducted amongst migrants in Singapore to improve national guidelines on screening and preventive treatment against LTBI.

This summary was prepared by Dr Yap Peiling, senior epidemiologist in the Department of Infectious Diseases, Tan Tock Seng Hospital.

We performed the first latent tuberculosis infection (LTBI) cross-sectional survey in Singapore, utilising the QuantiFERON Gold In-tube (QFT-GIT) assay. We also identified risk factors associated with LTBI. Household addresses of Singaporeans or Permanent Residents (PRs), aged 18-79 years, were identified and randomly selected. One eligible member per household was selected using the Kish grid. Each participant answered a questionnaire, comprising the medical history (including TB), socio-economic factors and lifestyle, and provided a blood specimen for the QFT-GIT assay. Participants with positive QFT-GIT results were defined as having LTBI if they were asymptomatic. To identify statistically significant risk factors, adjusted hazard ratios were obtained using the multivariable modified Breslow-Cox Proportional Hazard Model. An overall QFT-GIT positivity rate of 12.7% was detected in 1682 Singapore residents. This rate varied with the residents' country of birth. Higher LTBI prevalence was also significantly associated with increasing age, alcohol use and lower educational and socio-economic status.



Interview Functional Independence Measure score: self-reporting as a simpler alternative to multidisciplinary functional assessment

Vadassery SJ, Kong KH, Ho WML, Seneviratna A. Singapore Med J. 2019;50(4):199-201. doi:10.11622/smedj.2018048.

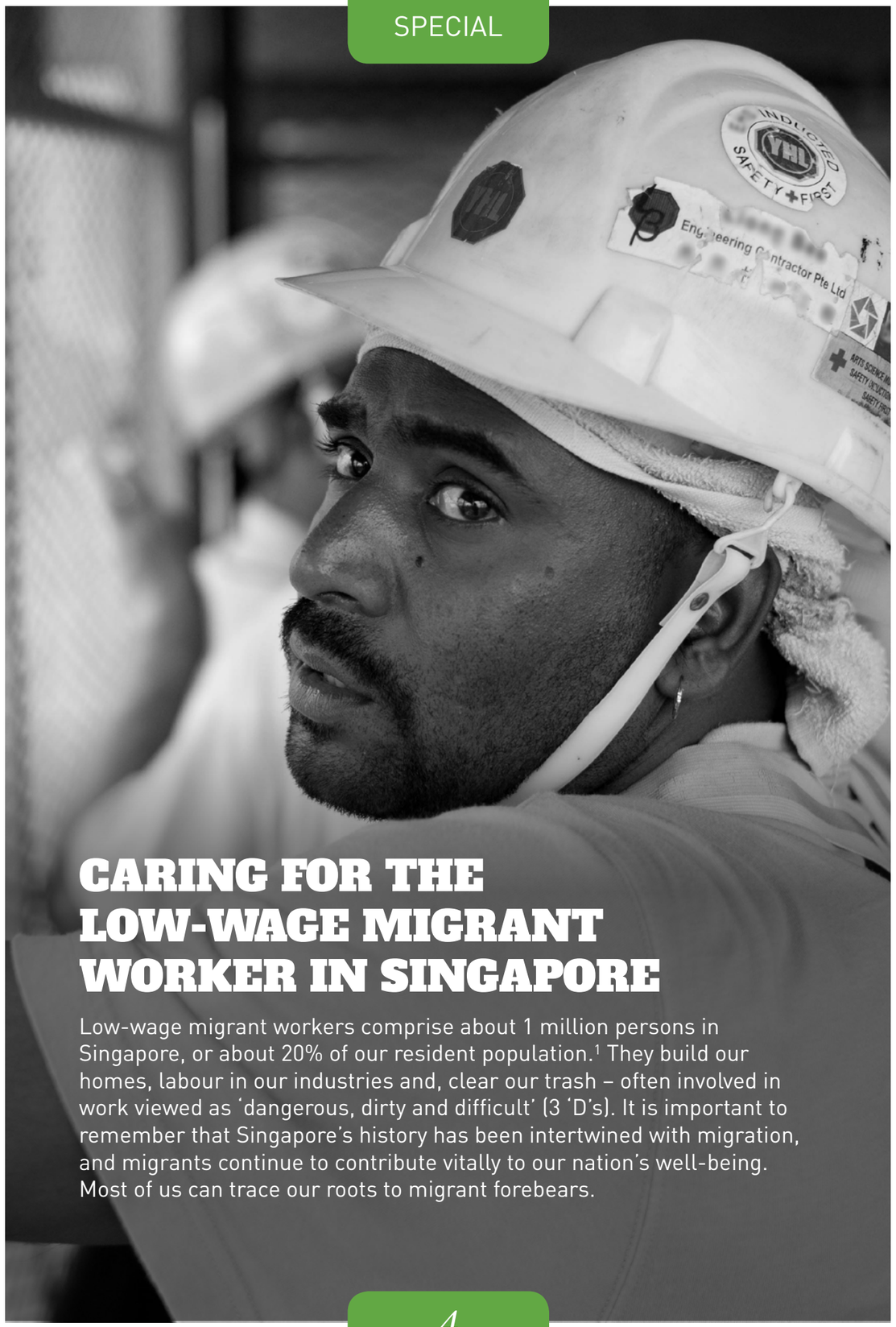
IMPORTANCE IN CLINICAL PRACTICE

FIM score is a validated, objective assessment of functional status commonly used in rehabilitation centres. This directly observed and performance-based assessment by a multi-disciplinary team, including a doctor, therapists and nurses, is considered the gold standard. However, it may not be feasible to conduct this for all patients due to time constraints. This study tested the validity of patient self-reported FIM-motor score in stroke patients as an alternative assessment tool in clinical practice. Our results show that patient self-reported scores can potentially be used as an alternative in stroke patients.

This summary was prepared by Dr Vadassery Shaji Jose, consultant in the Department of General Medicine, Tan Tock Seng Hospital.

This was a prospective, double-blind comparative study of the patient self-assessed versus the team-assessed standard Functional Independence Measure (FIM) algorithm. The study showed substantial agreement between the patient's self-reported score and total FIM motor score, with an intra-class correlation (ICC) of 0.651 (95% CI: 0.404–0.811). The individual items of motor scores also showed moderate to substantial agreement (ICCs ranging from 0.431 to 0.618), except that for eating, grooming, bathing, and dressing of lower body (ICCs <0.40). We conclude that patients' self-administered FIM motor score is a valid measure of functional ability, and may be useful in situations where multi-disciplinary FIM is difficult.

*TTSH Research News is curated and edited by **DR MELISSA TIEN**, consultant in the Department of Opthalmology, Tan Tock Seng Hospital.*



CARING FOR THE LOW-WAGE MIGRANT WORKER IN SINGAPORE

Low-wage migrant workers comprise about 1 million persons in Singapore, or about 20% of our resident population.[1] They build our homes, labour in our industries and, clear our trash – often involved in work viewed as 'dangerous, dirty and difficult' (3 'D's). It is important to remember that Singapore's history has been intertwined with migration, and migrants continue to contribute vitally to our nation's well-being. Most of us can trace our roots to migrant forebears.

As healthcare workers, our paths cross with migrants when they seek medical care in our field of practice. Migrants may find that culture and language pose barriers to receiving healthcare.[2] Other barriers may include healthcare costs, employer policies/practices and, ironically, healthcare workers (ourselves) – either through a lack of knowledge or indifference. It is important for healthcare workers to be aware of the provisions for migrant worker healthcare under Singapore law, and the various resources available to them. Nonetheless, healthcare workers should act always in the patient's best interest (migrant worker or not) and serve as advocates for this vulnerable population.

For more detailed guidance on treating migrant workers, readers may refer to a helpful article published by SMA.[3] Below, we highlight three main areas which healthcare workers in Singapore should be aware of.

1. Our duty of care for all patients, including migrant workers

Migrants may sometimes decline medical care due to concerns over the cost, duress from their employers, or fear of repatriation. This is especially pertinent where urgent care (e.g. life or limb/function-threatening illnesses or injuries) is needed. Regardless of the nature of illness or injury (whether work-related or not), and whether the treatment is outpatient or inpatient, the Employment of Foreign Manpower Act (EFMA) in Singapore mandates that employers are responsible for the upkeep and maintenance of their foreign employees in Singapore, including the provision of adequate food and medical treatment and, bearing the costs of such upkeep and maintenance.[4] This means that:

- Treatment (including investigations and admission decisions) should be based on best medical judgement, as one would do for any other patient.
- In cases where a letter of guarantee (which is sometimes required by an institution's Business Office) cannot be obtained in a timely manner, admission, investigation and treatment decisions should still proceed based on medical decision-making. Under the EFMA, employers of low-wage migrant domestic and non-domestic workers are mandated by law to provide medical insurance coverage of at least S$15,000 a year for inpatient fees and day surgeries. Employers may have to pay for a worker's admission prior to submitting insurance claims. If an employer declines to pay, the hospital's Business Office may lodge a complaint with the Ministry of Manpower (MOM).

CASE STUDY: A patient was seen at an outpatient specialist clinic for an undifferentiated fever (typhus versus dengue versus other causes of sepsis) requiring admission or close monitoring as an outpatient, with laboratory investigations to be performed either way. The worker expressed concerns over the cost, and wanted his employer to agree to the management plan. A call was made to the patient's work supervisor, who requested that all laboratory tests be performed at a polyclinic because he thought it was 'cheaper', and for the patient to be discharged. This was clearly not in the patient's best interest. The doctor-in-attendance explained that the investigations and treatments were medically-indicated; reminded him of the responsibilities of the employer under the EFMA which dictates that workers should have mandatory inpatient medical insurance coverage; and, reinforced to the supervisor that it was necessary for healthcare workers to act in the patient's best interest. Otherwise, it would be a contravention of the EFMA, and potentially reportable to the MOM. The supervisor acceded to the admission of his worker, who was subsequently diagnosed with, and treated for, murine typhus.

2. Adequate medical leave

The inadequacy of medical leave (both medical certificates (MCs) and hospitalization leave (HL)) for migrant workers has been in the news recently.[5] Doctors (especially those who may have contractual arrangements with employers) may feel coerced to shorten the duration of medical leave due to conflicts of interest. Employers are required to notify the MOM of work-related accidents that result in more than three days of sick leave. To avoid such paperwork, employers (and sometimes, even workers themselves) may ask doctors to shorten MCs or HL, leading to an inadequate recuperative period for workers.

Medical leave (MCs and HL) should be prescribed for adequate durations, and in consideration of medical factors. As most migrant workers are unaware of these provisions, and because cases of under-prescription of medical leave are generally undetected unless the authorities are notified, the onus is on healthcare providers to report to the Ministry of Health (Singapore Medical Council (SMC), 6372 3141; enquiries@smc.gov.sg) and MOM (Foreign Manpower Management Division, Occupational Safety and Health Inspectorate Department, 6438 5122 / 6317 1111; mom_oshd@mom.gov.sg) should they suspect cases of gross under-prescription. Alternatively, they should refer such cases to social workers at local, migrant worker non-governmental organizations (NGOs) for further evaluation.

CASE STUDY: In 2011, a migrant worker suffered hand and forearm fractures at a construction site accident, warranting two weeks' medical leave (a conservative estimate). After operating on him, the orthopaedic surgeon issued him only two days' MC, followed by a month of light duties. As the worker experienced pain after discharge, he went to a public hospital a week later where he was given HL for 19 days. This case was subsequently reported to the SMC via a local NGO. The Court then suspended the surgeon for six months for professional misconduct.[6]

3. Health resources for migrant workers

Outpatient costs (especially for chronic diseases) may be hefty for migrant workers as their insurance typically does not cover such costs, and hence these are often borne by the workers themselves.

There are several low-cost ($5-$10 for medications and consults) and free migrant healthcare clinics offering a variety of services (medical, dental, physiotherapy, social casework) which healthcare workers should be aware of, and refer their patients to, if necessary (table 1). You may even consider being a volunteer at these clinics!

ORGANIZATION	SERVICES	CONTACT DETAILS
HealthServe	• Subsidised medical and dental care • Social/ Casework • Counselling • Legal support • Social assistance such as free meals, subsidized transport, emergency shelter, and emergency fund	**Address:** Various locations (refer to website) **Website:** http://www.healthserve.org.sg/ **Phone:** 6743 9774 **Fax:** 6743 6174 **Email:** info@healthserve.org.sg
Karunya Community Clinic	• Subsidised medical care	**Address:** 668 Chander Rd, #01-16, Singapore 210668 **Phone:** 6338 3518
Caring Community Clinic	• Subsidised medical care	**Address:** 90 Race Course Rd, Singapore 218577 (Inside Foo Chow Methodist Church) **Phone:** 6293 8757 **Fax:** 6291 1412
Migrant Workers' Centre	• Social assistance such as shelter and food • Employment advice • Legal aid • Settling-in programmes	**Address:** 579 Serangoon Road, Singapore 218193 **Website:** http://www.mwc.org.sg/wps/portal/mwc/home **Phone:** 6536 2692 **Fax:** 6292 5305 **Email:** feedback@mwc.org.sg
Humanitarian Organization for Migration Economics (HOME)	• Helpdesk • Shelter • Medical Treatment • Legal Aid	**Address:** Various locations (refer to website) **Website:** https://www.home.org.sg/ **Phone:** 6741 1725
Transient Workers Count Too (TWC2)	• Social work assistance • Food programme • Medical subsidies	**Address:** 5001 Beach Road, #09-86, Golden Mile Complex, Singapore 199588 **Website:** http://twc2.org.sg/ **Phone:** 6247 7001 **Email:** info@twc2.org.sg

Table 1. Resources for Migrant Workers in Singapore.

As healthcare providers, we have an important role to play in the care of low-wage migrant workers. By being aware of the provisions under the law for such workers and, the resources available, we can provide better care for the migrants in our midst.

REFERENCES

1. *Ministry of Manpower, Singapore. Foreign workforce numbers. Available from http://www.mom.gov.sg/documents-and-publications/foreign-workforce-numbers. Accessed 17 February 2019.*
2. *Ang JW, Chia C, Koh CJ, et al. Healthcare-seeking behaviour, barriers and mental health of non-domestic migrant workers in Singapore. BMJ Global Health 2017;2:e000213.*
3. *Chan JSE and Chia D. Practical advice for doctors treating foreign workers. SMA News, February 2017. Available from: https://www.sma.org.sg/UploadedImg/files/Publications%20-%20SMA%20News/4902/Insight.pdf. Accessed 28 Jan 2019.*
4. *Ministry of Manpower, Singapore. Employment of Foreign Manpower Act (Chapter 91A). Employment of Foreign Manpower (Work Passes) Regulations 2012. Available from: https://www.mom.gov.sg/~/media/mom/documents/services-forms/passes/wpspassconditions.pdf. Accessed 17 February 2019.*
5. *The Straits Times (published 1 February 2019). Surgeon who did not give sick leave fights conviction. Available from: https://www.straitstimes.com/singapore/surgeon-who-did-not-give-sick-leave-fights-conviction. Accessed 17 February 2019.*
6. *TODAY (published 11 May 2016). Doc suspended over inadequate MCs for foreign worker. Available from: https://www.todayonline.com/singapore/landmark-ruling-against-doctor-ngos-say-inadequate-mcs-migrant-workers-still-problem. Accessed 17 February 2019.*

***DR SHAWN VASOO** is a senior consultant in the Department of Infectious Diseases, Tan Tock Seng Hospital.*

TREATMENT OPTIONS FOR HEPATITIS B

An estimated 240 million people around the world are chronically infected with hepatitis B, with the largest disease burden in Africa and Asia.[1] This patient population is at risk of developing liver decompensation, cirrhosis and hepatocellular carcinoma. Singapore has a successful hepatitis B vaccination programme that has helped bring down the rates of seroprevalence from 5% to 6% in the 1980s to 3.6% in 2010, marking it as an "intermediate endemicity region" for hepatitis B prevalence.[2]

Natural history

Human hepatitis B virus (HBV) belongs to the *Hepadnaviridae* family of small, enveloped, primarily hepatotropic DNA viruses. In the host, the virus replicates and assembles exclusively in hepatocytes before the virions are released. Chronic HBV (CHB) infection is a dynamic process reflecting the interaction between HBV replication and the host immune response. Not all patients with HBV infection have CHB infection. The natural history of CHB infection can be divided into five phases, taking into account the presence of hepatitis B envelope antigen (HBeAg) and hepatitis B surface antigen (HBsAg), alanine aminotransferase (ALT) values, HBV DNA levels and eventually, the presence or absence of liver inflammation (table 1).[3]

	Phase 1: HBeAg-positive CHB infection	**Phase 2: HBeAg-positive CHB infection**	**Phase 3: HBeAg-negative CHB infection**	**Phase 4: HBeAg-negative CHB infection**	**Phase 5: Occult hepatitis B**
HBeAg	Present	Present	Negative (anti-HBe+)	Negative (anti-HBe+)	Negative (Usually anti-HBe+)
HBsAg	High	High	Low	Intermediate	Absent or low (+/- AntiHBs)
ALT	Normal	Raised	Normal	Raised and fluctuating	Normal
HBV DNA	>10^7 IU/ml	10^4–10^7 IU/ml	<2,000 IU/ml	>2,000 IU/ml	Absent or low-level cccDNA detected in liver
Liver inflammation	Minimal or none	Moderate to severe	Minimal or none	Moderate	+/-
Liver fibrosis	None	Progression to fibrosis	Minimal or none	Moderate to severe	+/- (see below)
Notes	• Rate of spontaneous HBeAg loss is very low; more frequent and prolonged in subjects infected perinatally.	• Most patients achieve HBeAg seroconversion and HBV DNA suppression, and enter the HBeAg-negative infection phase. • Others may fail to control HBV and progress to the HBeAg-negative CHB phase for many years.	• Low risk of progression to cirrhosis or HCC; • Progression to CHB, usually in HBeAg-negative patients, may occur. • HBsAg loss and/or seroconversion may occur spontaneously in 1–3% of cases per year.	• Most have HBV variants in the precore and/or the basal core promoter regions that impair or abolish HBeAg expression. • This phase is associated with low rates of spontaneous disease remission.	• HBsAg loss before the onset of cirrhosis is associated with a minimal risk of cirrhosis, decompensation and HCC, and an improvement in survival. • If cirrhosis develops before HBsAg loss, patients remain at risk of HCC (and therefore, HCC surveillance should continue). • Immunosuppression may lead to HBV reactivation in these patients.
Old terminology	Immune tolerant phase	Immune reactive HBeAg positive	Inactive carrier phase	Chronic hepatitis B	Occult hepatitis B

Table 1. The five phases of the natural history of chronic HBV (CHB) infection.

ALT, alanine aminotransferase; AntiHBe, antibodies against hepatitis B envelope antigen; AntiHBs, antibodies against hepatitis B surface antigen; cccDNA, covalently closed circular DNA; HBeAg, hepatitis B envelop antigen; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma.

Goals of therapy

The utopian idea of complete eradication of HBV infection is difficult to achieve as the covalently closed circular DNA (cccDNA) remains integrated with the nucleus of the hepatocytes. Thus, HBsAg loss or HBeAg seroconversion with viral suppression is a suitable surrogate of successful response to therapy because of improved survival, reduction in hepatocellular carcinoma (HCC) risk, and prevention of disease progression.[4-6]

The Asian Pacific Association for the Study of the Liver (APASL) 2016 goals of therapy are:

1) The global eradication of HBV infection by various strategies, including vaccination, treatment and prevention of transmission.
2) The goal of therapy for CHB infection is to improve quality of life and survival of the infected person by preventing progression of the disease to cirrhosis, decompensated cirrhosis, end-stage liver disease, HCC and death; and, prevention of transmission of HBV to others.

The APASL 2016 endpoints of therapy are:

1. In both HBeAg-positive and HBeAg-negative patients, the sustained off-therapy HBsAg loss, with or without seroconversion to anti-HBs *(ideal endpoint)*.
2. Induction of sustained off-therapy virological response in both HBeAg-positive (with sustained anti-HBe seroconversion) and HBeAg-negative patients *(satisfactory endpoint)*.
3. If sustained off-therapy response is not achievable, then a maintained virological remission (undetectable HBV DNA by a sensitive PCR assay) under long-term antiviral therapy in HBeAg-positive patients who do not achieve anti-HBe seroconversion, and in HBeAg-negative patients *(the next most desirable endpoint)*.

The European Association for the Study of the Liver (EASL) 2017 goals of therapy are:

1) To improve survival and quality of life by preventing disease progression, and consequently, HCC development.
2) To prevent mother to child transmission, hepatitis B reactivation, and the prevention and treatment of HBV-associated extrahepatic manifestations.

The EASL 2017 endpoints of therapy are:

1) The induction of long-term suppression of HBV DNA levels represents the main endpoint of all current treatment strategies.
2) The induction of HBeAg loss, with or without anti-HBe seroconversion, in HBeAg-positive CHB patients. This often represents a partial immune control of CHB infection.
3) A biochemical response defined as ALT normalisation should be considered as an additional endpoint, which is achieved in most patients with long-term suppression of HBV replication.
4) HBsAg loss, with or without anti-HBs seroconversion, is an optimal endpoint, as it indicates profound suppression of HBV replication and viral protein expression.

Indications for treatment

The indications for treatment are similar for both HBeAg-positive and HBeAg-negative CHB patients, and involve consideration of three criteria: serum HBV DNA levels, serum ALT levels and severity of liver disease (table 2). Indications for treatment should also take into account age, health status, family history of HCC or cirrhosis and, extrahepatic manifestations.

INDICATIONS	TREATMENT STRATEGY
Decompensated Hepatitis B	Treat immediately; consider liver transplant if no stabilisation
Compensated cirrhosis	Treat at any ALT level if: (i) HBV DNA >2,000 IU/ml, or (ii) Elevated ALT, and HBV DNA is detectable
Severe reactivation of chronic Hepatitis B (treat immediately)	Treat immediately; consider liver transplant if no stabilisation
Pregnancy	Initiate antiviral therapy in 3rd trimester in mothers with high viral load (>2 x 10^5 IU/ml) to reduce transmission risk to the baby (with passive and active immunisation at birth)
Hepatitis C co-infection	Treatment of HBV should be considered in patients who are being treated for hepatitis C with direct acting antivirals, due to the risk of HBV flare and reactivation

Table 2. Indications for treatment of hepatitis B infection.

Treatment recommendations for HBeAg-positive and HBeAg-negative CHB infections according to international guidelines are summarised in tables 3 and 4, respectively.

	AASLD	EASL	APASL
Treatment definitely recommended	• HBV DNA >20,000* • ALT >2 times ULN	• HBV DNA >20,000 • ALT >ULN • Liver biopsy showing moderate to severe inflammation or fibrosis	• HBV DNA >20,000 • ALT >2 times ULN
Treatment may be considered	• HBV DNA 2,000–20,000 • ALT 1–2 times ULN • Older than 40 years, or liver biopsy showing moderate to severe inflammation or fibrosis	• HBV DNA >20,000 • ALT <ULN, or liver biopsy showing moderate to severe inflammation or fibrosis	• HBV DNA >20,000 • ALT <ULN, and liver biopsy showing moderate to severe inflammation or fibrosis
Monitor (bloods, ultrasound, HBs level)	HBV DNA <20,000	HBV DNA <20,000	HBV DNA <20,000

Table 3. Treatment recommendations for HBeAg positive CHB infection according to international guidelines.

**HBV DNA in IU/ml.*
AASLD, American Association for the Study of Liver Disease; ALT, Alanine transaminase; APASL, Asian Pacific Association for the Study of the Liver; EASL, European Association for the Study of the Liver; HBs, hepatitis B surface antigen; ULN, upper limit of normal.

	AASLD	EASL	APASL
Treatment definitely recommended	• HBV DNA >20,000* • ALT >2 times ULN	• HBV DNA >2,000 • ALT >ULN • Liver biopsy showing moderate to severe inflammation or fibrosis	• HBV DNA >2,000 • ALT >2 times ULN
Treatment may be considered	• HBV DNA 2,000 – 20,000 • ALT 1–2 times ULN • Older than 40 years, or liver biopsyshowing moderate to severe inflammation or fibrosis	• HBV DNA >2,000 • ALT <ULN, or liver biopsy showing moderate to severe inflammation or fibrosis	• HBV DNA 2,000–20,000 • ALT 1–2 times ULN • Older than 40 years, or liver biopsy showing moderate to severe inflammation or fibrosis
Monitor (bloods, ultrasound, HBs level)	HBV DNA <20,000	HBV DNA <20,000	HBV DNA <20,000

Table 4. Treatment recommendations for HBeAg negative CHB infection according to international guidelines.

**HBV DNA in IU/ml.*
AASLD, American Association for the Study of Liver Disease; ALT, Alanine transaminase; APASL, Asian Pacific Association for the Study of the Liver; EASL, European Association for the Study of the Liver; HBs, hepatitis B surface antigen; ULN, upper limit of normal.

Treatment options

Currently, there are two main treatment options for CHB patients: treatment with a nucleos(t)ide analogue (NA) or with pegylated interferon alpha (PegIFNa) (figure 1). The latter offers the advantage of finite duration of therapy of 48 weeks, but its clinical use is limited by the numerous side effects, and it must be used cautiously in patients with cirrhosis. PegIFNa therapy is not recommended in cases of decompensated HBV. The NAs that have been approved in Singapore for HBV treatment include lamivudine (LAM), adefovir dipivoxil (ADV), entecavir (ETV), telbivudine (TBV), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF). TBV is not available in the United States. These can be further classified into those associated with low barrier against HBV resistance (LAM, ADV, TBV) and those with high barrier to HBV resistance (ETV, TDF, TAF). The latter are the preferred choices for treatment.

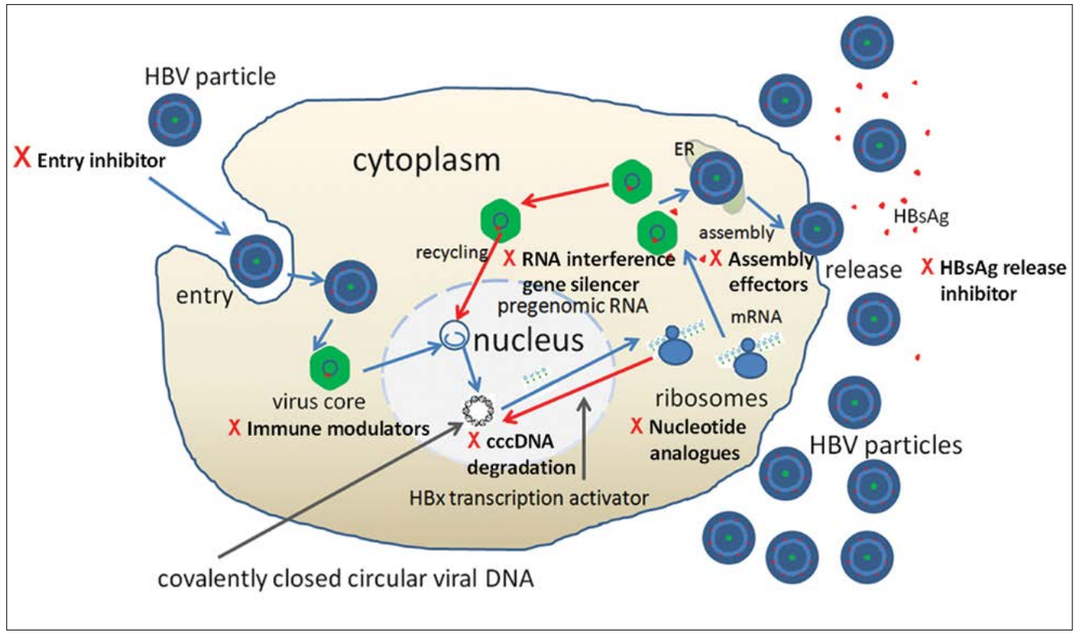


Figure 1. The hepatitis B virus life cycle and potential therapeutic targets (information obtained from Brahmania M et al[7]).

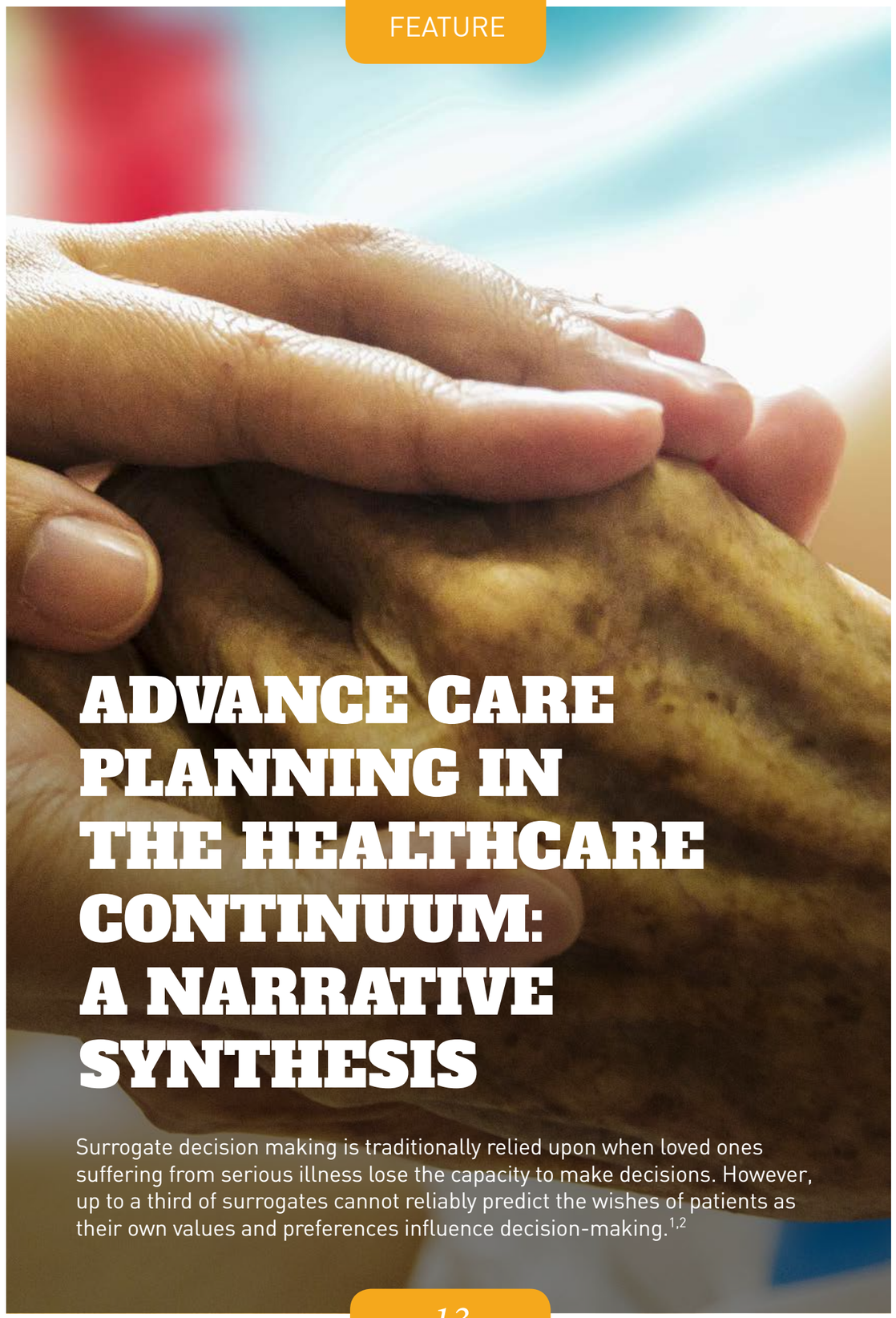
Conclusion

The use of high barrier to resistance antiviral drugs such as ETV, TDF and TAF have allowed physicians to treat patients with hepatitis B for many years, safely and effectively. True cure of HBV will need either elimination of cccDNA or prevention of transcriptional activity of cccDNA. But, this is rarely achieved with use of both NAs and IFN, and loss of HBsAg is seldom accomplished. Thus, most HBV patients need lifelong therapy. However, there is extensive current research focusing on achieving a cure for hepatitis B, by combining NA and IFN therapy, either in tandem or in sequence. Physicians are also attempting to cease treatment in HBeAg CHB patients who have achieved sustained suppression of viral load and are on long-term NA therapy. This is guided by quantification of HBsAg. In due time, one can hope to see an effective cure for hepatitis B, as well as hope for patients on long-term antivirals to safely and effectively stop therapy.

REFERENCES

1) Ott JJ, Stevens GA, Groeger J, et al. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine 2012; 30:2212–19.
2) Guan R. Hepatitis B virus infection in Singapore. Gut 1996; 38 Suppl 2:S13-17.
3) European Association for the Study of the Liver. EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection. J Hepatol 2017: 67:370–98.
4) Liaw YF, Sung JJ, Chow WC, et al, and the Cirrhosis Asian Lamivudine Multicentre Study Group. Lamivudine for patients with chronic Hepatitis B and advanced liver disease. N Engl J Med 2004; 351:1521–31.
5) Liaw YF. Impact of hepatitis B therapy on the long-term outcome of liver disease. Liver Int 2011; 31(suppl 1):117–21.
6) Fattovich G, Olivari N, Pasino M, et al. Long-term outcome of chronic hepatitis B in Caucasian patients: mortality after 25 years. Gut 2008; 57:84–90.
7) Brahmania M, Feld J, Arif A, et al. New therapeutic agents for chronic hepatitis B. Lancet Infect Dis 2016; 16:e10–21.

DR KALAIYARASI KALIYAPERUMAL
is a consultant in the Department of Gastroenterology & Hepatology, Tan Tock Seng Hospital.



ADVANCE CARE PLANNING IN THE HEALTHCARE CONTINUUM: A NARRATIVE SYNTHESIS

Surrogate decision making is traditionally relied upon when loved ones suffering from serious illness lose the capacity to make decisions. However, up to a third of surrogates cannot reliably predict the wishes of patients as their own values and preferences influence decision-making.[1,2]

There has been increasing advocacy for advance directives and advance care planning (ACP) over the past 20 to 30 years. ACP began as a movement in Western societies, following advances in medical science which prolonged lives with variable outcomes, as well as high-profile cases such as Terri Schiavo and Nancy Cruzan that forced society to ponder the meaning of keeping people alive physically when there is no hope of recovery. An aging society results in rising numbers of people with chronic progressive illness. The landmark SUPPORT study highlighted the poor quality of care at the end of life, and spurred additional research on decision making at this phase.[3] Factors considered important to patients, family and healthcare providers for a 'good' death include pain and symptom management, communication with one's physician, preparation for death, and the opportunity to achieve a sense of completion.[4] ACP is integral to this ideal.

Although legislative and regulatory bodies continue to promote advance directives, the overall prevalence of completed advance directives in the United States remains low.

In Singapore, ACP is not widely practised in the healthcare continuum. The Advance Medical Directive (AMD) Act was enacted in 1996. However, awareness and use of the AMD remains low, and it has limited impact on end-of-life decision making.[5]

The National Guidelines for Palliative Care released in 2014 advocates for all patients to have access to ACP at the end of life.[6] Clearly, there is a need to shift the perception of ACP as the completion of documents to it being a process of iterative conversations with patients and their loved ones. To achieve this, a comprehensive, flexible and systematic approach is required.

In 2009, the National Healthcare Group's End-of-Life Taskforce invited Respecting Choices, a renowned ACP faculty from Wisconsin, USA, to Singapore to train a group of healthcare professionals (HCPs) in ACP. In 2012, funding was disbursed through the Agency for Integrated Care to various regional health systems to run pilot projects in ACP. Since then, the practice of ACP has spread to all restructured hospitals, as well as some nursing homes, community hospitals, home care services and social care centres. In 2018, the total number of completed ACP documents nationally was 4,500; this is more than double the number from 2015.[7]

As awareness of, and interest in, ACP rises, this narrative synthesis sets out to examine a few questions of relevance.

What are the effects of ACP on end-of-life care?

ACP intervention outcomes are multidimensional and highly variable, depending on the studies and objectives of the investigators. Different types of ACP interventions have been studied in various settings and populations. Broadly, there is evidence that ACP influences end-of-life care in a positive way.

A systematic review on the effects of ACP on end-of-life care examined experimental and observational studies (with control groups) published between 2000 and 2012.[8] The authors reviewed 113 reports: 95% of the studies were observational; 81% originated from the United States; and, 49% were performed in hospitals (as opposed to 32% in nursing homes, 8% in the community, 10% in mixed settings and 1% in the outpatient clinic). ACP interventions in the form of do-not-resuscitate orders (39%) and written advance directives (34%) were most often studied. Do-not-resuscitate orders and do-not-hospitalise orders were found to decrease the use of life-sustaining treatment (including cardiopulmonary resuscitation measures), reduce hospitalisation rates, and increase the use of hospice and palliative care. Effects of advance directives (living wills and durable power of attorney) were more diverse but tended towards increased utilisation of out-of-hospital care to increase the patient's comfort, instead of life prolongation. Complex ACP interventions such as the Respecting Choices programme may be more effective than written documents alone, and were found to increase compliance with patient wishes and satisfaction with the level of care provided.

Patients who undergo facilitated ACP are more likely to have health directives.[9] Patients who prepared advance directives received care that was strongly associated with their preferences.[10]

A key Australian study published in 2010 randomised elderly patients to receive either a complex ACP intervention (Respecting Patient Choices) or no ACP.[11] Of the 56 patients who passed away within six months, end-of-life wishes were more likely to be known and followed in the intervention group (86%) compared to the control group (30%). In the intervention group, family members of patients who died reported to have experienced significantly less stress, anxiety and depression than those of the control patients. Patient and family satisfaction were higher in the intervention group.

Concern for self	• Autonomy: people value being in control of major life decisions • Meaningful existence: desire to maintain one's sense of dignity and respect • Quality of life: ability to enjoy everyday life • Likely outcome of treatment: the desire to understand and hope for chances of recovery • Burden to self and suffering: the desire to avoid suffering
Concern for others	• Burden to others: desire to avoid emotional and financial burden to loved ones • Input from others: views of loved ones are important influences on motivation to engage in ACP • Pressure from family: ACP can be viewed as a way for participants to exert their independence and actively counter the pressure they feel from others
Expectations about impact of ACP	• Trust in the medical system: varying degrees of trust or distrust in the medical system will influence participants' engagement in ACP • Predicted effectiveness: having information on the efficacy of medical treatments affected perceptions of the value of ACP
Anecdotes, stories and experiences	• Current events: stories in the media prompted participants to consider ACP and its relevance to their own situations • Emotional response to caregiving: stories from participants as well as what they heard from others about the difficulty of physically and emotionally supporting someone who was fragile and dying • Past experiences making decisions for others: witnessing the suffering of others and helping make decisions for them left strong impressions on participants

Table 1. Factors that influence individuals to engage in ACP.

Advanced cancer patients who report end-of-life conversations with their physicians were less likely to undergo mechanical ventilation and resuscitation, be admitted to or die in an ICU in their final week of life, as well as have significantly lower healthcare costs in their final week of life. There was also increased use of hospice and palliative care both in the outpatient and inpatient settings.[12] Caregivers reported that higher medical costs in the final week of life were associated with more physical distress (in the last week of life) and worse quality of death.[12]

What is the evidence of the net effects of ACP on cost of care? A recent systematic review found that facilitated ACP programmes have the potential to reduce net cost of care, although the impact depends on the details of the programme.[13] The primary goal of ACP programmes is to promote patient-centred care near the end of life, and not to reduce cost of care. To protect ACP discussions from undue influence of cost considerations, ACP programmes should invest in adequate training of facilitators, clear standards and transparent objectives.[13]

Overall, there is increasing evidence that ACP strengthens patient autonomy and improves quality of care near the end of life. Internationally, there is a need for studies with an experimental design in different settings, including in the community.

What factors influence people to engage in ACP as well as their views towards ACP?

Research shows that patients desire autonomy over end-of-life decisions, and expect physicians to initiate ACP conversations.[14,15]

A qualitative study in Pennsylvania looked at factors that influenced individuals to engage in ACP.[16] The study team conducted focus group discussions with 23 older individuals and grouped resulting themes into categories (table 1).

These finding suggest that HCPs may reinforce the benefits of ACP in promoting autonomy, dignity,

respect as well as patient-centred care, to encourage patients to engage in ACP. One can also help individuals to reflect on how ACP can alleviate the burden of decision-making on loved ones. Healthcare providers can draw on individuals' own experiences and observations regarding end-of-life experiences while facilitating ACP. The study also suggests that perceived benefits of ACP are related to views about its expected efficacy as well as the level of trust in the medical system.

In a qualitative study conducted locally amongst family caregivers of patients with advanced illness, there were similar views that ACP strengthens autonomy, improves quality of care at the end-of-life and prevents unnecessary suffering.[17] The caregivers also recognised that death is a reality of life, and that ACP helps one to prepare for this eventuality. These views on the perceived benefits of ACP were borne out in other studies as well.[18-21]

However, there are emotional and cultural barriers to discussing ACP for oneself and with loved ones.[17] Family caregivers express uncertainty over when and how to broach the topic. Some family caregivers struggle with the fear that open discussions about ACP may take away hope. There also exists a perception that it is not necessary to broach the topic of ACP when one is healthy, until the onset of advanced illness. This reticence to ACP and tendency to postpone making plans for oneself till one is older or in poorer health exists both in oriental and non-oriental cultures.[18-19,22]

Contrary to such perceptions, a study in patients with end-stage renal disease showed that patients were prepared to discuss end-of-life issues and their future medical care with their healthcare providers, and that facilitated ACP can enhance rather than destroy hope.[20]

Cultural views influence perceptions towards ACP as well. For example, some individuals believe in the traditional Chinese superstition that talking about death and dying is inauspicious and brings bad luck.[17] In the East Asian context, Confucianism and the relative importance placed on an individual's relations with family and society has a deep influence on decision-making, especially at the end-of-life.[17,23-24] This highlights the importance of the close involvement of family members and loved ones in the process of ACP.

Besides deferring to family members, patients may defer to physicians as they hold the belief that "doctors know best".[17] Other patient-cited barriers to completion of ACP include inconsistency with religious beliefs, ACP being viewed as a distressing topic, difficulty in completing documents, and indefinitely delaying the initiation of ACP.[25]

From these multidimensional views, it can be seen that ACP is a complex and iterative process. Successful ACP cannot be measured by the completion of advance directives alone; one should employ a tailored approach, taking into account individual readiness and attitudes as well as familial factors.[26-29] As an individual's preferences may change over time, there should be a regular review of one's attitude towards ACPs.

Some key shared constructs relevant to ACP include: perceived susceptibility (the belief that one is vulnerable to developing the condition the behaviour will protect against); self-efficacy; and, the barriers to and benefits of changing one's behaviour.[30]

The Transtheoretical Model, which explains stages of change as well as strategies at each stage to increase an individual's readiness for participation, may be a useful framework to utilise to engage people in ACP discussions.[31]

What are healthcare professionals' attitudes towards ACP discussions?

In a survey of HCPs in the United States, 72.6% of participants rated advance directives as fairly useful to very useful, while 58% noted that advance directives are followed most or all of the time.[32] Logistical challenges as to why advance directives are not followed include situations in which advance directives exist but are not available or not reviewed, or the relevance is unclear in relation to the condition of the patient. Process issues include conflict within the family regarding expressed wishes in advance directives, and disagreement between physicians and within the care team regarding prognosis and course of care. These highlight the importance of (i) a robust system to capture and transfer ACP information, as well as (ii) continuing education of HCPs on ethical and professional roles in applying advance directives to the clinical context of the patient.

In a local cross-sectional survey of physicians and nurses exploring the importance of factors influencing the end-of-life care decision-making of HCPs, respondents rated patients' wishes (96.6%), their clinical symptoms (93.9%), and patients' beliefs (91.1%) highly.[33] The majority (94.6%) of the HCPs would respect a competent patient's wishes over the family's wishes when treatment goals conflict. However, 59.9% of HCPs would abide by the family's wishes when the patient loses decision-making capacity, even if the patient's previously expressed wishes are known. This highlights that whilst end-of-life care decision-making by HCPs appears largely patient-centered, family members still wield significant influence. Thus, there is a need to closely involve family members in the process of ACP.

Most HCPs believe that ACP should be initiated upon admission to a health care facility, diagnosis of a terminal illness, delivery of news of a poor prognosis and the lead-up to a serious procedure.[32] In the same study, approximately 50% of HCPs indicated that annual, routine check-ups are an opportune time for this conversation.

Most physicians do not talk with their patients about their end-of-life wishes, and most report they would not discuss end-of-life options with terminally-ill patients who are feeling well; instead, they wait for symptoms or until there are no more treatments to offer.[34-36] In the outpatient setting, physicians often miss the opportunity to engage in ACP despite openers that patients provide that could have prompted such discussions.[37] The propensity to have such discussions may relate more to the personal preferences and level of comfort of patients, physicians, and family members, than to the health status of the patient.[34] Amongst renal HCPs locally, the main barriers for physicians were lack of time, concerns over family backlash, and the perception that patients were not prepared to discuss ACP.[38] Other physician barriers include perceived low health literacy of patients, lack of necessary skills, lack of privacy for discussion, and the consideration that the patient is not ill enough. The perceived lack of resources for ACP, lack of public awareness, and difficulties talking about death exist among nurses too.[39]

Whilst ACP would be most pertinent when a patient is diagnosed with serious illness, or deemed to have poor prognosis, it is not ideal to bring it up when the patient is stressed; it also undermines the principle of ACP as an iterative process of reflection. There needs to be systematic changes and educational impetus to bring the conversation upstream into outpatient clinics and when the patient is in better health.

What is the feasibility of ACP in primary care?

The primary care provider is well poised to hold ACP conversations with patients and families with whom he/she may have long standing relationships. ACP should be initiated early when patients are in better health, making the general practice setting ideal.

The local prevalence of ACP discussions amongst primary care providers is not known but likely to be very low.

Internationally, there is variable practice of ACP by primary care providers. ACP does not seem to be practised systematically for all community-dwelling older people, and is usually targeted at specific patient groups such as those with cancer, terminal illness, and dementia.[40] The topics discussed in ACP may vary from advance directives and psychosocial topics to exchanging opinions about situations that provide insight into the patient's end-of-life preferences. In general, primary care professionals do not practice ACP in a systematic way, and find it difficult to judge the right moment to start an ACP conversation.[41]

General practitioners (GPs) vary considerably in their conceptualisation of ACP in terms of the content of ACP discussions and tasks for the GP. This can lead to confusion as the role of GPs may vary according to how ACP is conceptualised. A shared conceptualisation is needed to ensure successful implementation of ACP.[42]

In a systematic review of barriers and facilitators for GPs to engage in ACP, the following were identified as key barriers: lack of skills to deal with patients' vague requests, difficulties with defining the right moment to initiate ACP, the attitude that it is the patient who should initiate ACP, and fear of depriving patients of hope.[43] Interestingly, studies have shown that patients believe it is the physician's responsibility to initiate ACP, suggesting a gap in expectation between patients and GPs.

Stronger evidence was found for the following facilitators: accumulated skills, the ability to foresee health problems in the future, skills to respond to a patient's initiation of ACP, personal convictions about who to involve in ACP, a longstanding patient – GP relationship, and the home setting. Initiation of ACP in general practice may be improved by targeting the GPs' skills, attitudes, and beliefs, but there should also be commensurate changes in health care organization and financing.[41]

To facilitate ACP in the primary care setting, there are ACP tools such as advance directives, and comprehensive programmes geared at improving end-of-life care in the generalist setting such as the Gold Standards Framework in the United Kingdom.[43]

In a systematic review of studies designedto increase advance directive completion in the primary care setting, the most successful interventions incorporated direct patient–healthcare professional interactions over multiple visits. Passive education of patients using written materials (without direct counselling) was a relatively ineffective method for increasing advance directive completion rates in the primary care setting.[44]

Some professionals have created innovative computer-based decision aids to empower individuals to reflect on their values, goals and healthcare wishes, and to outline a plan for how they wish to be treated.[45] Locally, patients may be directed to the Living Matters website for a conversation primer.[46]

For ACP implementation to be feasible in primary care, there needs to a combination of several interventions to systematize the initiation of ACP with patients:[47]

- Education of physicians;
- Systems to identify and trigger early discussions for eligible patients;
- Patient and family education;
- Structured formats to guide the discussions;
- Dedicated sections in electronic health records for recording information; and,
- Continuous measurement.

Conclusion

ACP strengthens patient autonomy, facilitates patient-centred care, and improves quality of care near the end of life. It helps to decrease the burden of decision-making of loved ones when patients are seriously ill. As an iterative process, it may also enhance mutual understanding and relationships between patients, their loved ones and their HCPs. There are multiple facilitators and barriers towards ACP in both patients and HCPs alike. It may be helpful to view ACP as a staged conversation requiring a tailored approach for each individual.

When an ACP system is implemented and improved over time, it is possible to achieve a high prevalence of advance care plans, which are then available to any HCP in any care setting. When these factors are achieved, it is possible to achieve a high rate of consistency between advance care plans and the treatment decisions made for the patient.[48]

Singapore is on the cusp of increasing awareness and interest in ACP. The challenge remains in making ACP a standard of patient-centred care at all points of the healthcare continuum.

Learning points

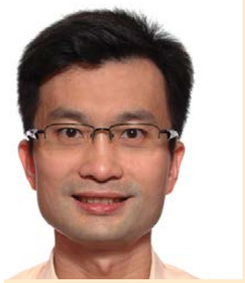
- ACP strengthens patient autonomy and improves quality of care near the end of life.
- Complex ACP interventions are more effective than written documents alone in improving ACP implementation.
- Patients and healthcare professionals hold multidimensional views towards ACP; interventions can be targeted at reinforcing facilitators and reducing barriers.
- Successful implementation of ACP entails systematic education of patients, engagement of stakeholders, training of healthcare professionals, an efficient system to capture ACP information, and continuous quality improvement.

Acknowledgement

This is an adaptation of an article written by the author which was originally published in the Singapore Family Physician 2016;42:7-12.

REFERENCES

1. *Shalowitz DI, Garrett-Mayer E, Wendler D. The accuracy of surrogate decision makers: a systematic review. Arch Intern Med 2006;166:493-497.*
2. *Vig EK, Taylor JS, Starks H, et al. Beyond substituted judgment: How surrogates navigate end-of-life decision-making. J Am Geriatr Soc 2006;54:1688–1693.*
3. *The SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). JAMA 1995;274:1591–1598.*
4. *Steinhauser KE, Christakis NA, Clipp EC, et al. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA 2000;284:2476-2482.*
5. *Tay M, Chia SE, Sng J. Knowledge, attitudes and practices of the Advance Medical Directive in a residential estate in Singapore. Ann Acad Med Singapore 2010;39:424–428.*
6. *Lien Centre for Palliative Care, Duke-NUS Graduate Medical School (2011). Report on the National Strategy for Palliative Care. Available from: https://www.duke-nus.edu.sg/docs librariesprovider12/news/report_on_national_strategy_for_palliative_care-4jan2012_0.pdf?sfvrsn=a4932aa0_0. Accessed 07 July 2016.*
7. *Primary Care Pages (2019). More Singaporeans opting for advance care plans. Available from: https://www.primarycarepages.sg/Pages/News/2019/More-Singaporeans-opting-for-advance-care-plans.aspx. Accessed 20 June 2019.*
8. *Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A. The effects of advance care planning on end-of-life care: a systematic review. Palliat Med 2014;28:1000-1025.*
9. *Schellinger S, Sidebottom A, Briggs L. Disease specific advance care planning for heart failure patients: implementation in a large health system. J Palliat Med 2011;14:1224-1230.*
10. *Silveira MJ, Kim SYH, Langa K. Advance directives and outcomes of surrogate decision making before death N Engl J Med 2010;362:1211-1218.*
11. *Detering KM, Hancock AD, Reade MC, et al. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. BMJ 2010;340:c1345.*
12. *Zhang B, Wright AA, Huskamp HA, et al. Health care costs in the last week of life: associations with end of life conversations. Arch Intern Med 2009;169:480-488.*
13. *Klingler C, in der Schmitten J, Marckmann G. Does facilitated Advance Care Planning reduce the costs of care near the end of life? Systematic review and ethical considerations. Palliat Med 2016;30:423-433.*
14. *Foo AS, Lee TW, Soh CR. Discrepancies in end-of-life decisions between elderly patients and their named surrogates. Ann Acad Med Singapore 2012;41:141-153.*
15. *Johnston SC, Pfeifer MP, McNutt R. The discussion about advance directives: patient and physician opinions regarding when and how it should be conducted. End of Life Study Group. Arch Intern Med 1995;155:1025-1030.*
16. *Levi BH, Dellasega C, Whitehead M, et al. What influences individuals to engage in advance care planning? Am J Hosp Palliat Care 2010;27:306-312.*
17. *Ng R, Chan S, Ng TW, et al. An exploratory study of the knowledge, attitudes and perceptions of advance care planning in family caregivers of patients with advanced illness in Singapore. BMJ Support Palliat Care 2013;3:343-348.*
18. *Samsi K, Manthorpe J. 'I live for today': a qualitative study investigating older people's attitudes to advance planning. Health Soc Care Community 2011;19:52–59.*
19. *Htut Y, Shahrul K, Poi PJ. The views of older Malaysians on advanced directive and advanced care planning: a qualitative study. Asia Pac J Public Health 2007;19:58–67.*
20. *Davison SN, Simpson C. Hope and advance care planning in patients with end stage renal disease: qualitative interview study. BMJ 2006;333:886.*
21. *Seymour J, Gott M, Bellamy G, et al. Planning for the end of life: the views of older people about advance care statements. Soc Sci Med 2004;59:57–68.*
22. *Kwak J, Salmon JR. Attitudes and preferences of Korean-American older adults and caregivers on end-of-life care. J Am Geriatr Soc 2007;55:1867–1872.*
23. *Tse CY, Tao J. Strategic ambiguities in the process of consent: role of the family in decisions to forgo life-sustaining treatment for incompetent elderly patients. J Med Philos 2004;29:207-223.*
24. *Ho MC. Sharing death and dying: advance directives, autonomy and the family. Bioethics 2004;18:87–103.*
25. *Sharda DR, Reid, Ronald DA. Completing an Advance Directive in the Primary Care Setting: What Do We Need for Success? JAGS 2007;55:277–283.*
26. *Briggs L. Shifting the focus of advance care planning: using an in-depth interview to build and strengthen relationships. J Palliat Med 2004;7:341–349.*
27. *Kolarik RC, Arnold RM, Fischer GS, et al. Objectives for advance care planning. J Palliat Med 2002;5:697–704.*
28. *Perkins HS. Controlling death: the false promise of advance directives. Ann Intern Med 2007;147:51–57.*
29. *Fried TR, Bullock K, Iannone L, et al. Understanding advance care planning as a process of health behavior change. J Am Geriatr Soc 2009;57:1547–1555.*
30. *Redding CA, Rossi JS, Rossi SR, et al. Health behavior models. Int Electronic J Health Educ 2000;3(Special Issue):180–193.*
31. *Prochaska JO, Velicer WF, DiClemente CC, et al. Measuring processes of change: applications to the cessation of smoking. J Consult Clin Psychol. 1988;56:520–528.*
32. *Bergman-Evans B, Kuhnel L, McNitt D, et al. Uncovering beliefs and barriers: staff attitudes related to advance directives. Am J Hosp Palliat Care 2008; 25:347-353.*
33. *Foo WT, Zheng Y, Kwee AK, et al. Factors considered in end-of-life care decision making by health care professionals. Am J Hosp Palliat Care 2013;30:354-358.*
34. *Kahana B, Dan A, Kahana E, et al. The personal and social context of planning for end-of-life care. J Am Geriatr Soc 2004;52:1163-1167.*
35. *Phua J, Kee ACL, Tan A, et al. End-of-life care in the general wards of a Singaporean hospital: an Asian perspective. J Palliat Med 2011;14:1296–1301.*
36. *Keating NL, Landrum MB, Rogers SO Jr, et al. Physician factors associated with discussions about end-of-life care. Cancer 2010;116:998-1006.*
37. *Ahluwalia SC, Levin JR, Lorenz KA, et al. Missed opportunities for advance care planning communication during outpatient clinic visits. J Gen Intern Med 2012;27:445-451.*
38. *Yee A, Seow YY, Tan SH, et al. What do renal health-care professionals in Singapore think of advance care planning for patients with end-stage renal disease? Nephrology 2011;16:232-238.*
39. *Jane S, Kathryn A, Sheila K. Implementing advance care planning: a qualitative study of community nurses' views and experiences. BMC Palliative Care 2010;9:4.*
40. *Glaudemans JJ, Moll van Charante EP, Willems DL. Advance care planning in primary care, only for severely ill patients? A structured review. Fam Pract 2015;32:16-26.*
41. *De Vleminck A, Houttekier D, Pardon K et al. Barriers and facilitators for general practitioners to engage in advance care planning: a systematic review. Scand J Prim Health Care 2013;31:215–226.*
42. *De Vleminck A, Pardon K, Beernaert K, et al. How do general practitioners conceptualise advance care planning in their practice? A Qualitative Study. PLoS One 2016;11(4):e0153747.*
43. *The Gold Standards Framework. Available from: www.goldstandardsframework.org.uk. Accessed 07 July 2016.*
44. *Ramsaroop SD, Reid MC, Adelman RD. Completing an advance directive in the primary care setting: what do we need for success? J Am Geriatr Soc 2007;55:277-83.*
45. *Making Your Wishes Known. Available from: https://www.makingyourwishesknown.com. Accessed 07 July 2016.*
46. *Living Matters Advance Care Planning. Available from: https://www.livingmatters.sg. Accessed 07 July 2016.*
47. *De Vleminck A, Houttekier D, Deliens L, et al. Development of a complex intervention to support the initiation of advance care planning by general practitioners in patients at risk of deteriorating or dying: a phase 0-1 study. Palliat Care 2016;15:17.*
48. *Hammes BJ, Rooney BL, Gundrum JD. A comparative, retrospective, observational study of the prevalence, availability and specificity of advance care plans in a county that implemented an advance care planning microsystem. J Am Geriatr Soc 2010;58:1249-1255.*



DR RAYMOND NG *is a senior consultant in the Department of Palliative Medicine, Tan Tock Seng Hospital.*

SPASTICITY MANAGEMENT

What is spasticity?

Spasticity is defined as a disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscle.

Spasticity forms one aspect of the upper motor neuron syndrome and it is important to realise that it can interact with other positive and negative features of an upper motor neuron syndrome to affect the function of the patient. Positive features include exaggerated tendon and primitive reflexes, spasms and clonus. Other positive features are spastic co-contraction, dystonia and associated reactions that can impact the patient's daily functioning. Some of the negative features of the upper motor neuron syndrome are weakness, reduced dexterity and reduced postural responses. The combination and interaction of these different aspects of the upper motor neuron syndrome, along with their functional consequences, make the management of spasticity challenging.

Spastic contraction refers to an excessive degree of simultaneous activity occurring in both the agonist and antagonist muscles during normal movement. This impedes voluntary movement. Spastic dystonia is a state of tonic muscle overactivity that occurs due to the inability of motor units to cease firing after a voluntary or reflex activity. Spastic dystonia can be inhibited by a tonic stretch maintained over several seconds which improves the ability to rest the muscle. Another behavioural manifestation of spasticity is the associated reaction, which are abnormal postural reactions observed in the affected side of hemiplegic patients.

Approach to treating spasticity

The approach to spasticity should be multidisciplinary and always begins with a comprehensive assessment. Spasticity may present as the initial symptom of a neurological illness. However, the more common situation is a patient with a long-term neurological condition who develops symptoms from worsening of spasticity. These can manifest as a worsening of function (e.g. falls or deteriorating mobility), an increase in care needs for activities of daily living, pain, involuntary movements (e.g. clonus or spasms), and stiffness.

> The clinical management of spasticity should be patient-centred and goal-oriented as part of the rehabilitation management strategy. Spasticity can be associated with complications such as contractures, pain, falls, and pressure ulcers. On the other hand, it may also have a positive impact on patients as a result of functional and mechanical advantages that come about from the increased tone in the muscle.

It is important to take a proper history to identify the presence of any trigger factors that can worsen the spasticity. These would include noxious stimuli from pressure sores, tight clothing, impacted stools, bladder dysfunction (urine retention or detrusor overactivity), and fractures. Spasticity can also be worsened during any systemic infection. In some patients with a chronic spinal cord injury, a change in spasticity may be the important presenting sign of syringomyelia.

Pain can increase spasticity and therefore it is important to address the generators or sources of pain. Pain can be musculoskeletal or neuropathic in nature. Musculoskeletal pain arises from unwarranted stress on the joint structures as a result of altered distribution of body weight in combination with soft tissue changes in patients who have upper motor neuron syndrome. Neuropathic pain can arise from lesions within the central nervous system that create a disturbance in sensory input. Such potential triggering factors should be addressed as part of the initial management of spasticity.

Assessment scales

As part of the initial assessment, clinical scales are used during the physical examination of the patient to evaluate the severity of the spasticity. One of these is the commonly used Modified Ashworth Scale (MAS). The MAS measures the degree of muscle tone through the sensation of resistance felt as the clinician passively moves a joint through its full range of motion (ROM). It is scored as follows:

0	No increase in muscle tone with ROM
1	Slight increase in muscle tone with or without a catch and release at the end of the ROM
1+	Slight increase in muscle tone followed by slight resistance through the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM
3	Considerable increase in tone making passive movement difficult
4	Affected parts rigid in flexion or extension

A point to note when using the MAS is the challenge in distinguishing between neural versus peripheral contributions to the increase in muscle tone during the passive ROM. In upper motor neuron syndrome, weakness and positioning of limbs can result in the muscles being immobilised at short lengths. This results in sarcomere shortening followed by the replacement of muscle and elastic tissue with connective tissue and

fat. These local biomechanical changes in the muscles are responsible for the development of contractures which can also be felt as an increase in tone (peripheral component) when utilising the MAS. However, unlike spasticity, contractures do not show dynamic changes like a catch or variation of tone with the speed at which the muscle is stretched. This is one way to distinguish between contractures and spasticity. It is useful to make this distinction as the non-pharmacological measures (which we describe later) can have a larger impact on treating contractures while the drug interventions are more effective at addressing the spasticity.

There are also other practical assessment scales besides the MAS that can help to guide the clinician when managing spasticity. For example, monitoring pain on a numerical rating scale, ambulation distance or gait speed are other practical techniques to quantify the functional goals when treating spasticity.

A goal attainment scale can be set up amongst patients and their treating healthcare team. The results of the intervention are scored from -2 to +2 as follows:

0	Outcome as expected
+1 to +2	Outcome better than expected
-1 to -2	Outcome worse than expected

This is a more relevant method of assessing treatment as the task and goals can be individually identified to suit the patient. The goals to be achieved can also be individually tailored to the patient around their current and expected levels of performance.

Management

The clinical management of spasticity should be patient-centred and goal-oriented as part of the rehabilitation management strategy. Spasticity can be associated with complications such as contractures, pain, falls, and pressure ulcers. On the other hand, it may also have a positive impact on patients as a result of functional and mechanical advantages that come about from the increased tone in the muscle. This occurs in situations when it allows them to stand or walk when their weakness would otherwise not permit this. Other benefits of the increased tone are maintaining muscle bulk, promoting venous return and reducing the incidence of orthostatic hypotension and osteoporosis. It is important to bear in mind that the benefits of treating spasticity should be weighed against its usefulness.

Some of the broad therapeutic goals to achieve when treating spasticity would be to:
- Improve functionality or motor control;
- Reduce disability or burden of care;
- Improve hygiene/skin care e.g. in the axilla, palm and perineal areas;
- Reduce pain;
- Prevent complications e.g. contractures or pressure ulcers; and
- Reduce spasms (which may affect sleep at night or make it difficult to do transfers).

The strategies for managing spasticity range from non-pharmacological options (involving physiotherapy and orthotics) to various pharmacological interventions and surgical procedures for appropriate cases.

Non-pharmacological strategies

Several non-pharmacological strategies have been used to address spasticity such as:
- **Muscle stretching.** Stretching of the muscles helps to improve the visco-elastic properties of the muscle-tendon unit and reduce the risk of muscle-tendon injury.
- **Muscle strengthening and re-education.** These help to improve motor control and function. Contrary to conventional beliefs, they do not worsen the spasticity.
- **Physical modalities.** Various physical modalities such as shock wave therapy, cryotherapy, thermotherapy, and ultrasound therapy have also been used to reduce spasticity. They act by increasing local metabolism, circulation and improving the extensibility of connective tissue. Neuromuscular electrical stimulation has also been used to help reduce spasticity. Physical modalities should be used with caution in patients who have a decreased ability to communicate (e.g. aphasia) or insensate dermatomes as they may have limited ability to detect the adverse effects of treatment and communicate them to the clinician.
- **Serial casting.** The maintenance of the position of a limb to provide a prolonged period of stretch, via casting, has been shown to increase joint ROM. It should be done by an experienced physiotherapist in a serial manner every 2 to 3 days to stretch out the soft tissue and/or lengthen the muscle. This usually requires frequent monitoring and re-evaluation to look out for adverse effects such as pain, skin breakdown or neurovascular compromise.
- **Use of orthotics.** Orthoses are generally used in conjunction with other interventions including physiotherapy, positioning, stretching, oral anti-spasticity medication, and botulinum toxin injections. The various orthotics and indications for their prescription are elaborated below.

Orthotics

A thorough assessment of the specific impairments causing disability is necessary for appropriate prescription. An orthotist is the primary clinician responsible for the prescription, manufacturing and

management of orthoses. An orthosis may be used to control, guide, limit, and/or immobilise an extremity, joint or body segment for a particular reason and to restrict movement in a given direction. When referring patients, the doctor should provide enough clinical detail to help the orthotist prescribe the most appropriate device. Orthoses are prescribed in patients with lower limb spasticity with the aim of:
- Decreasing muscle spasticity by increasing muscle length through providing a prolonged stretch and exerting an inhibitory effect through sensory stimulation
- Breaking up mass patterns of movement
- Improving biomechanics and stability.

Figure 1. Night resting ankle-foot orthosis.

Some typical orthoses that achieve these aims are detailed below. The first is a night resting splint that can be used to reduce and/or prevent contractures whilst at rest (figure 1). It is usually worn all night if the patient can tolerate it.

Most patients who have suffered a stroke tend to develop dorsiflexion weakness. Orthotic devices for these patients reinstate normal heel contact and provide ground clearance when walking. For patients with a mild flaccid foot drop, most prefabricated devices can be used (figure 2).

The prescription criteria are:
- Weakness or paralysis of the dorsiflexors
- Normal plantar flexor function
- Good medio-lateral stability of the subtalar and midtarsal joints in stance
- Good control of the hip and knee
- No spasticity.

Equinus caused by spasticity in the plantarflexor muscles of the foot will require a greater amount of corrective control than a flaccid drop foot. The hyperactivity of the muscles means that a type of

Figure 2. Posterior Leafspring ankle-foot orthosis.

thermoplastic ankle-foot orthosis (AFO) that is more rigid than a Posterior Leafspring will be required (figure 3). Conventional designs of orthoses block plantarflexion although some allow dorsiflexion. Care must be taken when considering allowing dorsiflexion as it is known that stretching of the plantarflexor muscle group may elicit a spastic response, and this should be avoided in cases where there is high tone.
- The prescription criteria are:
- Moderate to high tone in the gastrocnemius muscle
- Less than 10 degrees of ankle dorsiflexion with the knee in maximum extension
- Moderate to severe medio-lateral instability at the ankle
- A requirement to provide proximal control at the knee and hip joints.
- A design feature of an orthosis to manage spasticity is extending the sole to create a full sole plate. The sole plate should be aligned in such a way that the toes are held in a few degrees of extension.

Figure 3. Solid ankle-foot orthosis

The solid or rigid AFO does not allow ankle motion at the talocrural, subtalar and midfoot joints. The solid AFO enables heel strike during the stance phase and toe

clearance during the swing phase. It can also improve knee stability and provide control of varus or valgus deformities. The addition of wedging to the solid AFO allows the orthotist to tune the biomechanical effect and enable improved neuromuscular function.

There exists a huge range of orthotic appliances, including various types of AFOs for management of spastic equinus or equinovarus deformity at the ankle, contracture correction devices and tone inhibiting insoles. The input of an experienced orthotist is invaluable in the assessment and selection of the appropriate orthosis. However, adequate clinical information and aim of the referral should be provided to facilitate this.

Pharmacological Management

The choice, timing and dose of oral medications for treatment of spasticity should be optimised according to specific goals. Medication should be started at low dosages and gradually up-titrated in small increments. It is important to regularly review the effects of these medications and gradually taper them off if they are not effective. Sudden discontinuation of these medications should be avoided to prevent a rebound increase in spasticity. It can sometimes be useful to combine drugs at a lower dosage for more effective treatment while minimising the adverse side effects.

Some of the first-line medications used for managing spasticity are baclofen, gabapentin, pregabalin, and tizanadine. The main side effects to watch out for are drowsiness and dizziness. The medications are prescribed this way:

- Baclofen: Starting dose of 5 mg twice to three times a day. Dose can be increased by 5 mg every 5 to 7 days. Maximum dose can be up to 80 mg/day.
- Gabapentin: Starting dose of 100 to 300 mg daily. Maximum dose can be up to 3600 mg daily divided into three doses.
- Pregabalin: Starting dose of 25 to 50 mg daily. Maximum dose of up to 600 mg daily in two divided doses.
- Tizanidine: Starting dose of 2 mg daily. Maximum dose of up to 36 mg daily in three divided doses. Need to look out for side effects of dry mouth and postural hypotension. Monitoring of the liver function test is also required.

The benzodiazepine group of drugs, such as diazepam, can also be used to manage spasticity. However, it would be preferable to avoid them as first-line medication in view of tolerance, dependency and withdrawal syndromes. They can also cause drowsiness, reduced attention and memory impairment. The long half-life and exacerbation of cognitive impairment tend to limit its usefulness in patients with stroke and traumatic brain injuries. Clonazepam, though, can be quite helpful especially for treating nocturnal spasms. The benzodiazepines are used this way:

- Diazepam: Starting dose of 2 mg daily. Maximum dose of up to 40 to 60 mg daily in three or four divided doses.
- Clonazepam: Starting dose of 0.25 mg to 0.5 mg usually at night. Maximum dose up to 2 mg once at night.

Dantrolene is another useful medication to consider as it acts peripherally by supressing the release of calcium from the sarcoplasmic reticulum of skeletal muscle. The main side effects are anorexia, nausea and vomiting. Monitoring the liver function is essential as it can cause hepatic failure, although rarely. Dantrolene is prescribed this way:

- Dantrolene: Starting dose of 25 mg daily. Maximum dose of up to 400 mg daily in four divided doses.

The reduction of spasticity that occurs with treatment may unmask an underlying weakness that could be present from the upper motor neuron syndrome. This can have an effect on the patients' postural stability and function. Patients should be cautioned on this undesirable effect and it is useful to get caregivers on board to assist the patient or be alert during this period to reduce risk of falls.

If the spasticity is confined to a single limb or a few small muscles, then focal treatment can be considered. Focal pharmacological treatment consists of intramuscular botulinum toxin injections or peripheral alcohol blocks.

Botulinum toxin is more commonly used for treatment of focal spasticity. It acts by blocking the pre-synaptic release of acetylcholine at the neuromuscular junction. Botulinum toxin injections have very low incidence of systemic effects compared to oral medications. Serious adverse effects are uncommon and include unintentional weakening of the targeted or surrounding muscles, bleeding or nerve trauma. The onset of action is within 24 to 72 hours, with the effect peaking around 2 weeks post-injection. The duration of effect from intramuscular botulinum toxin injections is around 3 to 4 months. It is during this window period where other neurorehabilitative approaches like physiotherapy, splinting or electrical stimulation should be used to enhance its effects. It is also important for the botulinum toxin injections to be given in the context of a clear goal of treatment.

Peripheral nerve blocks are a form of chemical neurolysis aimed at eliminating the neurological input responsible for spastic activity. They are usually targeted at peripheral nerves or motor points and the procedure is done with the aid of a peripheral nerve stimulator.

Temporary nerve blocks can be achieved through the use of lignocaine or bupivacaine and these usually last about 1 to 6 hours. Temporary nerve blocks are usually employed for the clinician to assess the impact on function before deciding whether to proceed to a long-term solution. A more sustained effect can be obtained with ethyl alcohol (50%) which results in the destruction of neural tissue through protein coagulation. The clinical effect of a sustained nerve block can only last for up to a year as partial nerve regeneration and sprouting can occur. Some of the side effects include pain during the injections and local muscle necrosis. It is preferable to target predominantly motor nerves as dysesthesia can occur with the destruction of sensory nerve fibres. Commonly targeted are the obturator nerve (for reduction of adductor spasticity to aid in perineal hygiene and catheter care), the posterior tibial nerve (for equinovarus deformities) and the musculocutaneous nerve (for elbow flexor spasticity).

Surgical Options

If spasticity is generalised and difficult to control, intrathecal therapies can be considered. Relatively small doses of baclofen administered intrathecally can achieve high concentrations within the spinal cord. This can produce the therapeutic effect of relaxing the muscles while minimising the systemic side effects. A 50-mcg test dose is usually administered via a lumbar puncture or temporary catheter in adults. If this is clinically assessed to be efficacious, the pump can be subcutaneously implanted in the abdomen and the baclofen delivered via a catheter into the subarachnoid space. Intrathecal baclofen is not without risk of complications. Abrupt withdrawal of intrathecal baclofen due to a pump failure or a blocked catheter can result in a clinical emergency. The baclofen withdrawal syndrome manifests as a high fever, rebound spasticity and confusion, which can be life-threatening. Therefore, this is a modality of treatment that requires a coordinated approach with regular monitoring by an experienced team.

Neurotomies may be performed in the peripheral nervous system to obtain more permanent results than can be accomplished with an alcohol nerve block. During this procedure, the target nerve is selectively exposed and transected. When spasticity results in deformities or contractures in the limbs, tendon release and transfers can be considered. These involve procedures like a tendo-achilles release for plantar flexor contractures and a split anterior/posterior tibial tendon transfer for the correction of ankle inversion. These procedures can aid in allowing for better function (e.g. improving weight bearing and balance through the lower limbs during standing or transfers) and reducing the incidence of complications like pressure sores.

Summary

Spasticity is a common feature that can be encountered in a variety of long-term neurological conditions like stroke, spinal cord injuries or traumatic brain injuries. It can be associated with pain, affect the function of patients and increase their care needs. Spasticity can be quite challenging to treat and the cornerstone of management involves a collaborative multidisciplinary approach.

FURTHER READING

1. Stevenson VL, Playford D. Neurological rehabilitation and the management of spasticity. Medicine 2016; 44(9):530-536.
2. Setiota NO, Kong KH. Practical approach to spasticity. In: Handbook of Rehabilitation Medicine. 2017; 147-158.
3. Gozum MALP, Rosales RL. Botulinum toxin A therapy in early post stroke spasticity: providing a wider treatment avenue. Int J Neurorehabilitation 2016;3:207.
4. Nair KPS, Marsden J. The management of spasticity in adults. BMJ 2014; 349:g4737.

DR DESHAN KUMAR S/O RAJESWARAN *(left) is a consultant in the Department of Rehabilitation Medicine, Tan Tock Seng Hospital.* ***MR TREVOR BRIAN BINEDELL*** *(right) is a principal prosthetist/orthotist in the Foot Care & Limb Design Centre, Tan Tock Seng Hospital.*

THE ROLE OF SPEECH THERAPY IN DEMENTIA

As the population of Singapore is ageing, diseases associated with old age are expected to rise. One of these, dementia, is increasing at a rapid rate.

The Singapore Alzheimer's Disease Association projected that the number of individuals aged 65 years and above with dementia will increase by more than three times, from 53,000 in 2020 to 187,000 by 2050.[1]

Another worrying issue, according to the National Neuroscience Institute, is the alarming rate of younger people being diagnosed with the disease.[2] 'Young onset dementia' refers to the onset of dementia before the age of 65. The number of individuals with young onset dementia has increased 4.5 times, from 27 in 2011 to 121 in 2016.

Most people see dementia as a condition associated predominantly with memory loss and forgetfulness. But for many individuals with early-onset dementia, communication and behaviour are the first areas to be affected. This in turn significantly impacts their ability to engage socially and to work.

In this article, we specifically look at the changes in communication in individuals with dementia and how speech therapy can benefit the sufferers.

How dementia affects communication

Dementia is an umbrella term that describes a wide range of symptoms such as failing memory, deterioration of intellectual and language function, and personality change. It is caused by cell death and tissue loss, as a result of abnormal build-up of plaques and tangles of protein in the brain or previous brain insults such as strokes. The types of dementia include Alzheimer's dementia (AD), vascular dementia (VD), frontotemporal dementia (FTD), Lewy body dementia (LBD) and dementia associated with Parkinson's and other related diseases.[3]

Communication is defined as a process by which information is exchanged between individuals through a common system of symbols, signs or behaviour.[4] It can be verbal through speech and language or non-verbal through written language (reading, writing), gestures, facial expressions, vocal tones, and body language.

Cognition and language have to work hand in hand to enable an individual to communicate effectively. Communication difficulties arise in individuals with dementia as a result of cognitive or language impairment.

Cognition includes abilities such as attention, memory, organisation, executive function, and problem solving. Progressive decline of cognitive function in individuals with dementia may impact communication, and the difficulties that arise are termed cognitive communication deficits.

Language is the ability to encode ideas into words or symbols for communication with someone else and involves speaking, comprehending, reading, and writing. Language should be differentiated from speech, which is the motor aspect of spoken language. Impairment in language is a common finding among individuals with dementia and can be a presenting symptom in all forms of dementia depending on the brain areas affected.

Language is impacted when the brain's language centres responsible for language comprehension and production, namely, Wernicke's area in the temporal lobe and Broca's area in the frontal lobe, are affected by the spread of the disease. Hence, individuals with FTD present with predominantly language difficulties initially.

Communication difficulties that arise as a result of language impairment are termed aphasia. In patients with dementia, apahsia is usually progressive.

Cognitive changes in dementia and possible impact on communication

An individual who does not have good attention will not be able to focus on the topic of communication and hence will not respond appropriately.

Dementia patients with declining memory may not understand conversations as they do not remember the information that has been conveyed. They may also have difficulties finding words as they cannot remember and retrieve relevant words in the conversation.

Reduced attention and memory also impact an individual's ability to learn and acquire new information. Poor organisation skills impair the structuring of ideas when communicating with others, leading to tangential responses in conversations or even disorganised speech. Table 1 summarises the cognitive communication difficulties that individuals with dementia may face.

Language changes in dementia

How and when language problems develop depends on the individual, as well as the type and stage of dementia.

Receptive language impairment

Individuals with dementia may have difficulty understanding what a communication partner tells them as they cannot process the information received in the brain. This is especially so for long and abstract sentences. They might also have difficulty with reading words, sentences or paragraphs.

Expressive language impairment

Individuals with dementia may have trouble finding the right word, tend to repeat words and phrases, or become 'stuck' on certain sounds.

They may not be able to find the right word (e.g. 'book' instead of 'newspaper'), use substitutes for words (e.g. 'thing to sit on' instead of 'chair') or may not find any word at all. They may continue to have fluent speech, but without any meaning. For example, they might

DIFFICULTIES IN…	POSSIBLE EXAMPLES
Memory/Attention	• Forgetting instructions/ conversations • Word finding difficulties • Reduced ability to acquire new information
Social Skills (Pragmatics)	• Responds inappropriately • Poor turn taking
Reasoning & Problem Solving	• Difficulty in processing nuances in language • Difficulty in understanding abstract language e.g. idioms, jokes
Organisation	• Tangential and disorganised speech

Table 1. Summary of possible cognitive communication impairment scenarios.

jumble words, combining, truncating and forming words that do not make sense.

If they also have receptive language impairment, they may not respond appropriately because they do not understand what was said or meant.

Individuals with dementia might also have acquired dysgraphia, a difficulty in spelling words and forming grammatically accurate sentences in writing.

The famous writer Iris Murdoch showed hints of dementia in her last novel "Jackson's Dilemma" as the range in vocabulary declined compared to novels written at her peak.[5] She was formally diagnosed with dementia two years after publication of the book. Figure 1 shows the different stages of dementia and possible language deficits at each stage.

Speech therapy for individuals with dementia

Speech therapists are equipped to help individuals with dementia in the areas of swallowing and communication, which includes language and cognitive communication impairment.

However, individuals with dementia are more often referred to speech therapists to manage swallowing difficulty rather than for communication problems. There is a lack of awareness of the role of a speech therapist in a patient whose language and cognitive function declines in dementia. Due to the progressive nature of dementia, it is difficult to accurately gauge how effective speech therapy would be in improving communication in these individuals.

EARLY	MODERATE	LATE
• Mild difficulty with word finding • Mild difficulty with abstract/ complex concepts • Beginning to progressively decrease in vocabulary	• Reduced talking/social skills • Difficulty understanding complex sentences/ instructions • Poor naming abilities • Poor vocabulary • Increased use of stereotypical sentences eg. "I don't know" • Impaired interaction during conversation • Difficulty maintaining topics	• Incoherent, irrelevant speech • Repetitive speech • Difficulty initiating/responding to conversation • Eventually no meaningful speech • May become mute

Figure 1. Stages of dementia and possible language deficits.

In recent years, as the population has become more educated and the profile of the ageing population has changed, the focus of healthcare has shifted towards patient-centred care. In keeping with this, helping individuals with dementia maintain independence is becoming increasingly important. At the centre of this shift, communication plays a crucial role, hence referrals to speech therapists for improving communication is slowly becoming more common.

Assessment

When an individual with dementia is first referred to a speech therapist, the therapist begins by taking a collaborative case history from the individual and the accompanying family members. Information such as cognitive ability, level of social interaction and education, and communication history is gathered.

Formal and/or informal assessments are carried out to assess cognition, and receptive and expressive language ability at different levels e.g. single word, sentence and paragraph, as well as in different modalities – auditory, reading, writing, and speaking. Results of the assessment allow the speech therapist to diagnose if an individual has cognitive communication or language deficits.

Following assessments, the therapist discusses possible therapy plans and goals with the individual with dementia and his/her family.

Therapy and management of language impairment

Language therapy can be divided into two approaches: impairment-based and activity/participation (functional)-based. Impairment-based therapy targets specific impairments observed with the aim of maintaining or restoring declining function. Activity/ participation (functional)-based therapy usually does not target a specific impairment but serves to maximise the individual's residual language ability to enable them to participate in activities of daily living and function in daily settings.

Evidence for language therapy for individuals with dementia and progressive aphasia has been scarce but is slowly emerging. It has been observed that the language complaints in progressive aphasia can be quite similar to that in stroke-induced aphasia. Croot et al. advocate that speech therapists apply decisions about therapy for individuals with progressive aphasia based on knowledge and evidence obtained from stroke-related aphasia.[6] However, the nature of progressive aphasia requires the speech therapist to make necessary adaptations to therapy approaches and modify treatment goals over time.

It is difficult to cover therapy and management of all aspects of language impairment within this article. We focus on word-finding difficulty, an early and common

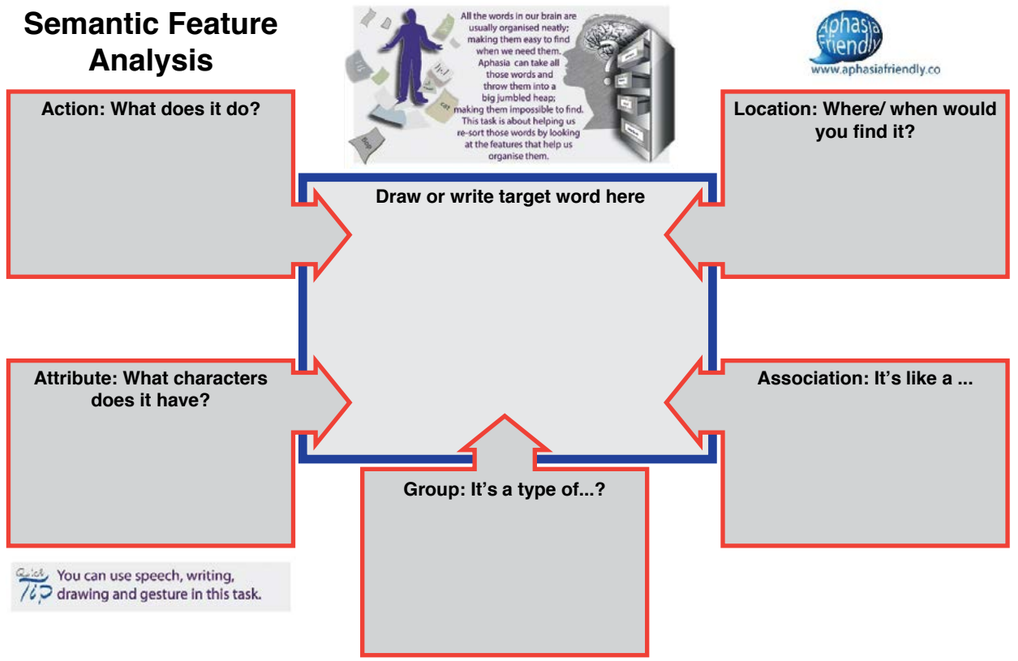


Figure 2. Sample of a semantic feature analysis chart used during treatment (obtained from www.aphasiafriendly.co.).

issue when working with individuals with dementia and one which has a huge impact on communication.

Word-finding: Impairment-based therapy

For individuals with word-finding difficulty, an example of impairment-based therapy is targeting naming at the single word level. There are many therapy tasks that could target naming e.g. object-to-picture matching, single-word-to-object matching, object naming with cueing hierarchy, and/or semantic feature analysis.

During the assessments, the speech therapist determines if difficulty in word retrieval reflects a *semantic* (meaning based) or phonological impairment (based on auditory or articulatory word forms). The level of impairment(s) identified will then determine which task(s) to choose.

For example, if an individual faces difficulty in retrieving the name of an object because he/she forgets the meaning of the object, the speech therapist may engage the individual in a semantic feature analysis task which involves the description of semantic features (e.g. function, physical attributes, location, etc.) of the target object in a systematic way (figure 2). These associations allow the neural networks surrounding the name of the target object to be activated to a greater extent, hence increasing the chances of it being retrieved.[7]

Besides therapy tasks, the speech therapist also considers the method to approach the tasks in individuals with progressive aphasia. One of the more commonly used approaches is the spaced retrieval method.

Individuals with dementia often have memory difficulties so it may be difficult for them to monitor and correct their responses or retain information learnt. In the spaced retrieval method, individuals are asked to recall target items with increasing time intervals and errors are monitored. It is an errorless learning technique which aims to enable individuals with dementia to have accurate learning and improve retention of information.

Word-finding: Activity/participation (functional)-based therapy

The more frequently used therapy tasks would include script training, circumlocution using principles of semantic feature analysis and conversation training for communication partners.

In script training, individuals with progressive aphasia may develop written scripts together with their speech therapists to facilitate speech for specific functional contexts that is relevant to them (e.g. describing their condition to friends).[8] Script training involves intensive drilling practice over a few sessions, either via oral reading or computer-based systems to increase automaticity in functional contexts.

We have briefly discussed semantic feature analysis as an impairment-based therapy task. It can also be used as a functional-based therapy task. Individuals with progressive aphasia can be taught to compensate for word-finding difficulty for target objects in conversations by describing their semantic features (e.g. physical attributes, function, location where the objects would be found, etc).[9,10] As mentioned previously, this may eventually prompt some of them to make the connections and retrieve the target word from their mental lexicon. If not, it aids communication partners in guessing the target that they have in mind, reducing the chances of a communication breakdown.

Conversation training for communication partners helps them understand the facilitators and barriers of conversation.[11] Together with individuals with progressive aphasia, communication strategies (e.g. use of cueing hierarchy, asking appropriate questions, use of visual aid or gestures) are explored to improve the effectiveness of their communication. As dementia progresses, the affected individual might lose their ability to communicate verbally. In that situation, the individual might need to rely totally on non-verbal communication e.g. gestures, tones, drawing or low technology communication aids[12] such as a picture communication chart (figure 3) to facilitate communication.

Therapy and management of cognitive communication impairment

Cognitive difficulties which are in the domain of our neuropsychology colleagues might significantly impact communication, hence there is some overlap with the domain of speech therapy. A multidisciplinary team approach which involves a speech therapist and a neuropsychologist can be considered when delivering the therapy.

Therapy for cognitive communication impairment tends to be more dynamic, with greater focus on functional strategies to support communication in a specific task as there is, inevitably, continued cognitive decline for individuals with dementia. As dementia progresses, the individuals might have difficulties with motivation or limited learning abilities and this makes formal impairment therapy tasks inappropriate.

The following sections discuss some common cognitive communication difficulties and potential strategies to overcome them.

Figure 3. Examples of picture communication charts to depict grooming activities (left) and items associated with daily living (right).

Social skills – Pragmatics

During the milder stage of dementia, some individuals may already have developed subtle difficulties in social skills, e.g. in turn taking or tangential speech, although they may not realise it yet. Therapy can be targeted at improving self-awareness and monitoring through education, video feedback and role play with communication partners. The individual has to be assessed to determine if he/she has sufficient retained awareness and memory to be able to apply internal monitoring. If not, the communication partner might benefit more from the therapy as it will help them understand reasons for communication breakdown and also enhance self-awareness to facilitate communication with the individual.

Memory

A speech therapist can help the individual with dementia come up with a memory and communication book to support memory and conversation. The book is useful as it acts as a source of information or a means to convey information about the individual.

It is important to train the individual and their communication partners to use the book as an aid. Errorless and spaced retrieval techniques mentioned earlier can also be used in this context to train the individual.

As memory decline progresses, the goals of therapy might change over time. Instead of engaging in daily functional conversation, the goal might have to shift towards just engaging the individual to promote intra- and interpersonal functioning and improve well-being. Reminiscence therapy, the process of recalling episodes from one's past, capitalises on remote autobiographical memory that most individuals with dementia would likely to have preserved. It allows them to continue interaction with others, hence reducing social isolation.[13] As the individual engages in reminiscence therapy, a life story book, which is a book that depicts the life history of a person in chronological order, containing pictures and personal memorabilia, can be created in the process. A pilot randomised controlled trial showed that creation of a life story book resulted in positive psychosocial impact on individuals with dementia and their caregivers.[14] Crook et al. also demonstrated that life story books were associated with an improvement in well-being and communication abilities, and led to positive changes in behaviours.[15]

Education for communication partners

Main communication partners of individuals with dementia include family members, caregivers and healthcare workers. They play a very important role in facilitating conversation as they do not face the cognitive or language limitations that individuals with dementia face.

Frequent communication breakdown might lead to deterioration in the mood and well-being of both the individual and the communication partners. Caregivers and family members might also be at risk of caregiver burden and stress. Hence, one of the key roles of speech therapists is to provide education, support and training to maximise their communication with individuals with dementia.

A group at the University of Queensland first developed the MESSAGE Communication Strategies in Dementia for Care Staff (table 2) to improve home care staff and caregivers' knowledge about communication strategies and reduce the negative impact of providing care to individuals with dementia.[16-18] The programme has been positively received and has greatly improved knowledge and confidence of dementia carers.

Besides the MESSAGE strategies, the speech therapist is able to advise on more specific strategies based on the findings of their assessment and the goals of the individuals with dementia as well as their caregivers/family.

M	**Maximise** attention
E	Watch **Expression** and body language
S	Keep it **Simple**
S	**Support** their conversation
A	**Assist** with visual aids
G	**Get** their message
E	**Encourage** and **Engage** in communication

Table 2. MESSAGE communication strategies
(Information obtained from Conway & Chenery, 2016)[16]

Conclusion

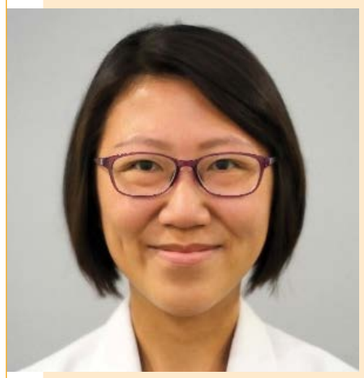
Speech therapists play an important role in helping individuals with dementia maintain an optimum level of communication and social connectedness, especially in the earlier stages of dementia before significant decline in language and cognitive abilities set in. Doctors are encouraged to refer dementia patients for assessment by a speech therapist the moment early signs of communication difficulties are encountered.

Although there remains much to be done in developing language and cognitive communication therapies for this group of individuals, there is emerging evidence that speech therapy can help to improve communication.

However, it is also important for us to recognise that for individuals with dementia, communication goals need to be reviewed and expectations adjusted as the condition progresses. It is also crucial to educate and prepare them and their caregivers for disease progression early. This will address any misconceptions and maintains realistic expectations of the individuals' communication abilities.

REFERENCES

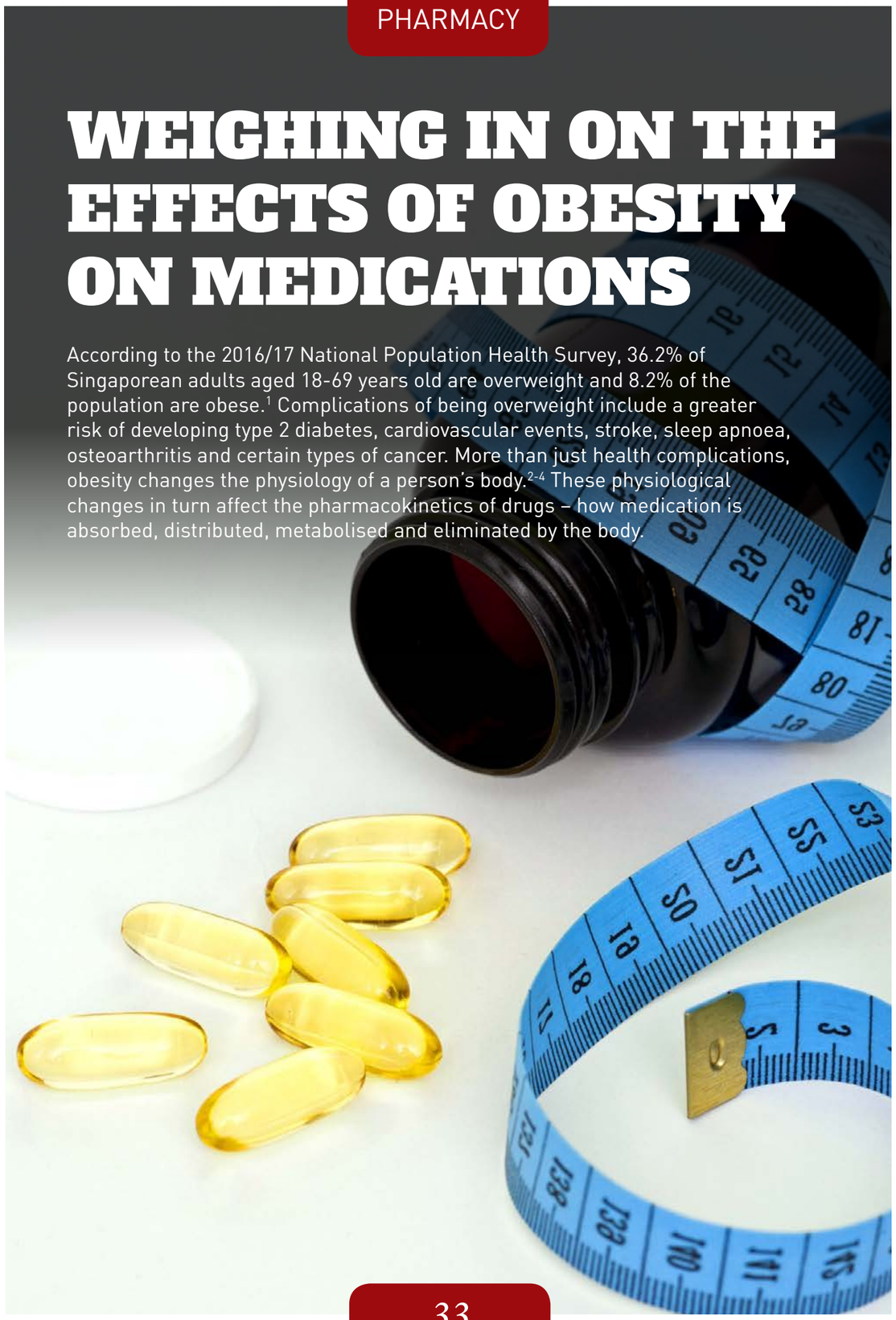
1. *Alzheimer's Disease Association. Dementia in Singapore. 2017. Available from: http://alz.org.sg/dementia/singapore/.*
2. *Gan E. Dementia affecting more people under the age of 65. Singapore: TodayOnline; 2017. Available from: http://www.todayonline.com/singapore/dementia-affecting-more-people-under-age-65.*
3. *Types of dementia. [Online]. USA: National Institute on Aging; 2017. Available from: https://www.nia.nih.gov/health/types-dementia.*
4. *Serra A, Vaquerizo B, Miranda F. Dior eluting balloon: The spanish dior registry: Focus on small vessels.*
5. *Hopkin M. Iris murdoch's last book reveals early alzheimer's. Nature, News; 2004. Available from: https://www.nature.com/news/2004/041129/full/news041129-4.html.*
6. *Croot K, Nickels L, Laurence F, Manning M. Impairment- and activity/participation-directed interventions in progressive language impairment: Clinical and theoretical issues. Aphasiology. 2009;23(2):125-60.*
7. *Boyle M. Semantic feature analysis treatment for aphasic word retrieval impairments: What's in a name? Top Stroke Rehabil. 2010;17(6):411-22.*
8. *Kaye RC, Cherney LR. Script templates: A practical approach to script training in aphasia. Top Lang Disord. 2016;36(2):136-53.*
9. *Maddy KM, Capilouto GJ, McComas KL. The effectiveness of semantic feature analysis: An evidence-based systematic review. Ann Phys Rehabil Med. 2014;57(4):254-67.*
10. *Davis L, Stanton S. Semantic feature analysis as a functional therapy tool. Contemp Issues Commun Sci Disord. 2005;32:85-92.*
11. *Simmons-Mackie N, Raymer A, Cherney LR. Communication partner training in aphasia: An updated systematic review. Arch Phys Med Rehabil. 2016;97(12):2202-21.e8.*
12. *Pattee C, Von Berg S, Ghezzi P. Effects of alternative communication on the communicative effectiveness of an individual with a progressive language disorder. Int J Rehabil Res. 2006;29(2):151-3.*
13. *Subramaniam P, Woods B. The impact of individual reminiscence therapy for people with dementia: Systematic review. Expert Rev Neurother. 2012;12(5):545-55.*
14. *Subramaniam P, Woods B, Whitaker C. Life review and life story books for people with mild to moderate dementia: A randomised controlled trial. Aging Ment Health. 2014;18(3):363-75.*
15. *Crook N, Adams M, Shorten N, Langdon PE. Does the well-being of individuals with down syndrome and dementia improve when using life story books and rummage boxes? A randomized single case series experiment. J Appl Res Intellect Disabil. 2016;29(1):1-10.*
16. *Conway ER, Chenery HJ. Evaluating the message communication strategies in dementia training for use with community-based aged care staff working with people with dementia: A controlled pretest-post-test study. J Clin Nurs. 2016;25(7-8):1145-55.*
17. *Smith ER, Broughton M, Baker R, Pachana NA, Angwin AJ, Humphreys MS, et al. Memory and communication support in dementia: Research-based strategies for caregivers. Int Psychogeriatr. 2011;23(2):256-63.*
18. *Liddle J, Smith-Conway ER, Baker R, Angwin AJ, Gallois C, Copland DA, et al. Memory and communication support strategies in dementia: Effect of a training program for informal caregivers. Int Psychogeriatr. 2012;24(12):1927-42.*



MS AUDREY TEH YUFEN *is a senior speech therapist in the Department of Speech Therapy, Tan Tock Seng Hospital.*

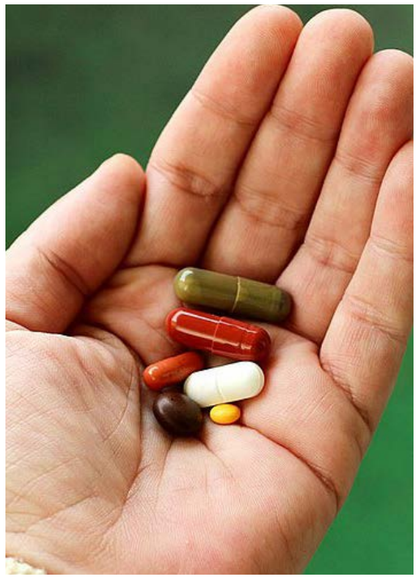
WEIGHING IN ON THE EFFECTS OF OBESITY ON MEDICATIONS

According to the 2016/17 National Population Health Survey, 36.2% of Singaporean adults aged 18-69 years old are overweight and 8.2% of the population are obese.[1] Complications of being overweight include a greater risk of developing type 2 diabetes, cardiovascular events, stroke, sleep apnoea, osteoarthritis and certain types of cancer. More than just health complications, obesity changes the physiology of a person's body.[2-4] These physiological changes in turn affect the pharmacokinetics of drugs – how medication is absorbed, distributed, metabolised and eliminated by the body.



Definition and Assessment of Obesity

The World Health Organisation (WHO) definition for being overweight and obese is body mass index (BMI) greater than 25 kg/m² and 30 kg/m², respectively.[5] BMI is calculated by dividing a person's weight in kilograms (kg) by the square of his/her height in metres (m). However, due to variances in the body-fat composition in Asian populations, an equivalent risk of cardiovascular comorbidities is seen at a lower BMI compared to a Caucasian counterpart.[6] As such, the definitions by Singapore's Ministry of Health for being overweight and obese are BMIs higher than 23 kg/m² and 30 kg/m², respectively.[7]



In clinical settings, BMI is a practical method for assessing body fat as it provides a more accurate measure of total body fat compared to the assessment of body weight alone. However, clinicians should be aware of the limitations of BMI as an indicator of body-fat composition. For example, BMI overestimates body fat in individuals who are overweight but very muscular (e.g. body builders) and in individuals who are fluid-overloaded. BMI can also underestimate body fat in individuals who have very little muscle mass (e.g. elderly with muscle loss associated with aging).[8]

Although there are other accurate methods to measure body fat such as dual-energy x-ray absorptiometry (DEXA) scanning, these are impractical and expensive for routine use.[9]

Physiological Changes in Obesity and Effects on Pharmacokinetics

Obesity presents a challenge for clinicians as changes in physiology alter the pharmacokinetic properties of drugs. Consequently, drug dosing may have to be individualised, with special attention to drugs with weight-based dosing or narrow therapeutic indices.

Absorption

Absorption of a drug is affected by the rate of gastric emptying, gut permeability and the amount of drug left after intestinal and hepatic metabolism. It is one of the factors affecting time for peak absorption and the concentration of drug attained in the serum.

In obese populations, gut permeability is increased and gastric emptying is accelerated, which may lead to greater intestinal absorption of drugs. However, there are only a few studies on the effect of obesity on drug absorption, with the data suggesting that there is no significant difference in drug absorption between obese and lean individuals.[4]

Distribution

Drug distribution in the body is represented by the volume of distribution (V_d), a primary pharmacokinetic parameter that relates drug concentration measured in plasma or blood to the amount of drug measured in tissues. Drugs with extensive tissue uptake generally have larger V_d. The V_d of drugs is dependent on several factors such as lipophilicity and hydrophilicity of the drug, ionisation properties of the drug, availability of protein for drug binding, and blood to plasma ratio of the patient.[2]

As obesity increases both fat and lean mass, with a higher percentage increase in fat mass per kilogram than lean mass, a drug with greater lipophilicity would theoretically have a larger volume of distribution in obese patients as it diffuses readily into adipose tissues. On the contrary, there is little to no change in the V_d of drugs with greater hydrophilicity as they are expected to remain in aqueous components such as blood and plasma.

This increase in V_d in obese populations is observed with highly lipophilic drugs such as benzodiazepines and thiopental.[10] However, lipophilicity does not necessarily predict changes in V_d in all drugs. For example, digoxin, cyclosporine and propofol, which are highly lipophilic, do not show an increase in V_d in obese individuals.[2]

It is unclear if protein binding affects the distribution of drugs as data from studies have been contradictory. Major plasma proteins responsible for drug binding are albumin and α1-acid glycoprotein (AAG), which bind acidic drugs and basic drugs, respectively.[4] Studies have shown that the binding of drugs (e.g. thiopental and phenytoin) to albumin is similar in both obese and non-obese individuals. However, the binding of drugs to AAG has been reported to either increase or decrease in obesity, with debatable effects on unbound drug fractions.

In summary, the effect of obesity on V_d is variable, and is difficult to predict based on drug lipophilicity alone since the affinity of each drug for excess adipose tissue is unique.

Metabolism and Elimination

Unlike V_d, the chemical attributes of a drug have little impact on drug clearance (CL) as this parameter is largely affected by hepatic and renal physiology. CL is an essential pharmacokinetic parameter to consider when devising a maintenance dose regimen as it is inversely related to a drug's elimination half-life.[3] Elimination half-life ($t_{½}$) refers to the time it takes for drug plasma concentration to be reduced by 50%, and may be calculated using the formula: $t_{½} = (\ln 2 \times V_d)/CL$.

Clearance of medication is dependent on blood flow to the liver, kidneys and the availability of enzymes for metabolism. Obesity has been linked to non-alcoholic fatty liver disease and hepatic blood flow may be altered by the accumulation of fat in the liver, which in turn might have an impact on hepatic drug CL.

However, hepatic clearance has been reported to be unchanged or even increased in obese patients. Hepatic drug metabolism is generally classified into phase I and phase II reactions, and the former is mostly mediated by cytochrome P450 (CYP) enzymes. While some animal and in vitro human studies have reported a decrease in CYP3A4 metabolism, some studies suggest an increase in CYP2E1 metabolism. Whereas, for phase II metabolism involving conjugation pathways, glucuronidation and sulfation, metabolism has been reported to be unchanged or increased in obesity.[2]

As mentioned, the clearance of a drug is also dependent on renal function. The relationship between renal function and obesity is complex. While obesity has been reported to increase glomerular filtration rate (GFR) and renal plasma flow, it is also a risk factor for the development of chronic kidney disease (CKD).[11,12] In the clinical setting, the most commonly used formula for estimating GFR is the Cockcroft-Gault (CG) formula, which is used to calculate creatinine clearance (CrCl). Most drug dosing adjustments for renal function are based on CrCl, and most pharmacokinetic studies have relied on the CG equation to stratify patients' severity of CKD.[13] However, there are caveats to using this formula to estimate renal function in the obese population as it has not been validated for use in obese patients.

The CG formula was developed using data from 249 patients who were all within 10% of lean body weight, and uses serum creatinine concentration, weight, age, and sex to estimate creatinine clearance:

$$\text{CrCl} = \left[\frac{(140 - age) \times body\ weight\ (in\ kg) \times 88.4}{[serum\ creatinine\ (\frac{umol}{L})] \times 72}\right] \times 0.85\ (\text{if female})].$$

In the obese population, this formula has been shown to overestimate CrCl when total body weight is used. On the contrary, using ideal body weight results in underestimation of CrCl, as obese patients are expected to have a greater total lean body weight compared to a normal weight individual of equivalent height.[10] While a possible solution to overcome this would be to use adjusted body weight to represent the gain in lean weight in between total body weight and ideal body weight, the validity of this approach has not been evaluated.[14]

In summary, obesity affects the pharmacokinetic profile of drugs due to changes in a person's physiology. A drug's pharmacokinetic profile may be broken down into four processes - absorption, distribution, metabolism and elimination. Within these four processes exist numerous factors that may alter the amount of drug that enters the body. Due to the profound effects that a single parameter change can cause, it is difficult to reliably predict how drugs are affected by obesity. As a result, it would be advisable to refer to specific pharmacokinetic studies of drugs to determine if a special dose recommendation is available for obese patients.

Practical Guide to Medications which require weight-adjusted dosing

At present, our knowledge of the influence of obesity on drug pharmacokinetics is limited, and there is no standard recommendation for drug dose adjustments in an obese population. For drugs that are dosed according to body weight, dose adjustments for

loading and maintenance doses may be adjusted based on data from studies that were carried out in the obese population. Drugs with a narrow therapeutic index should also be used prudently, and dose adjustments may be made with the help of drug plasma concentrations. Table 1 below lists some examples of drugs that require weight-adjusted dosing in obese patients:

Dosing recommendations in obese patients (BMI ≥ 30kg/m^2)					
Drugs	**IBW**	**TBW**	**ABW**	**Comments**	**References**
Anti-bacterials					
Aminoglycosides					
Amikacin			√	Consider dose capping at 2 – 2.5g	15, 16, 17, 18
Gentamicin			√	Consider dose capping at 480 – 640mg	15, 16, 17, 18
Neomycin			√		15, 16, 17, 18
Streptomycin			√		15, 16, 17, 18
Glycopeptide					
Vancomycin		√		Do not exceed 2g for loading dose. Nephrotoxicity risk is higher if total daily dose ≥ 4g. Monitor trough serum concentrations and adjust accordingly	15, 16, 17, 18
Sulfonamide derivative					
Trimethoprim/ Sulfamethoxazole				Limited data available. Inadequate oral doses (< 5mg/kg per 24H trimethoprim in divided doses) had worse outcomes in morbidly obese patients	15, 18
Anti-fungals					
Amphotericin B	√				19
Fluconazole		√			15, 19
Flucytosine	√				19
Voriconazole	√				19, 20
Anti-coagulants					
Enoxaparin		√		Treatment dose: Use TBW up to 150kg and monitor anti-Xa concentrations. VTE prophylaxis in bariatric surgery: BMI ≤ 50 kg/m² – 40mg 12H; BMI ≥ 50 kg/m² – 60mg 12H	16, 21, 22, 23
Heparin			√	Treatment dose: ABW for bolus and initial infusion rate. Subsequent doses based on APTT values	16, 21, 24
Anxiolytics					
Diazepam	Maintenance dose	Loading dose		Obese patients experience a longer half life	10, 16
Lorazepam	Maintenance dose	Loading dose		Obese patients experience a longer half life	10, 16
Midazolam	Maintenance dose	Loading dose		Obese patients experience a longer half life	10, 16
Anti-epileptics					
Phenytoin	Maintenance dose	Loading dose		Loading dose: Use 14mg/kg IBW + 19mg/kg for the weight in excess of IBW; or 1500mg for patients 125 – 150% IBW and 2,000mg for patients weighing more than 150% IBW	25, 26, 27
Valproic acid	√			Changes in body weight will affect clearance. Monitor concentrations	28

Table 1: Examples of drugs which require weight-adjusted dosing
IBW – Ideal body weight; TBW – Total body weight; ABW – Adjusted body weight; ABW = [0.4 x (TBW – IBW) + IBW]

Treatment of Obesity

In a bid to improve quality of life, clinicians should consider the prevention and management of obesity. Through weight loss, obese patients may reduce future health challenges and comorbidity risks.[4]

Lifestyle modification is recommended as the main treatment strategy for weight management. Pharmacotherapy, if used, should be an adjunct to behavioural modification to reduce food intake and increase physical activity. Treatment for obesity may be considered in patients with a BMI equal or greater than 30 kg/m^2, or greater than 27.5 kg/m^2 in Asians with comorbidities like hypertension or diabetes. Medical treatment should be considered only after patients fail to lose weight (at least 5% of total body weight at 3 - 6 months) through regular exercise (at least 150 minutes of exercise a week) and dietary modifications (consuming 500 kilocalories lesser than their estimated daily energy requirements).[7,29]

Pharmacologic options that are available locally for the treatment of obesity include liraglutide, orlistat, and phentermine. For patients who are candidates for drug therapy, the choice of drug should take into account patient's comorbidities, relative contraindications (if any), patient preference, cost and potential adverse effects.

Liraglutide

Liraglutide is an analog of human glucagon-like peptide-1 (GLP-1) which decreases inappropriate glucagon secretion and slows gastric emptying. Due to its beneficial effects on glycemia and reduction of major cardiovascular events in a clinical trial, it is the preferred choice in patients with diabetes.[30] Liraglutide is initiated at a dose of 0.6mg daily by subcutaneous injection, and may be increased by 0.6mg weekly up to a maximum of 3mg for up to 2 years. Treatment should be discontinued after 12 weeks on 3mg/day dose if patients have not lost at least 5% of their initial body weight.[31] Common side effects include diarrhoea, nausea, vomiting and an increased risk of hypoglycaemia and upper respiratory tract infection. Liraglutide is contraindicated in patients with a personal or family history of endocrine neoplasia syndrome and medullary thyroid carcinoma.

Orlistat

Orlistat, a non-systemic pancreatic lipase inhibitor, blocks the hydrolysis of dietary triglycerides into absorbable fatty acids and monoglycerides. Unabsorbed triglycerides and cholesterol are then excreted via the faeces, reducing approximately 25 - 30% of calories ingested as fats.[14] The recommended dose of Orlistat is 120mg three times a day within 1 hour of a fat-containing meal. It may be considered for long-term therapy (up to 4 years). Although some studies have shown benefits in lowering lipids and decreasing blood pressure, the use of orlistat is frequently limited by the side effects of flatulence, soiling from anus, steatorrhoea and backache. As patients cannot absorb fat-soluble vitamins from their food, they are recommended to supplement their diet with vitamins A, D, E and K at least 2 hours before or after taking orlistat.

Phentermine

Phentermine is a sympathomimetic amine with similar pharmacologic activity to the prototype anorectic drug, amphetamine. The exact mechanism of action is not established, although it appears to exert its appetite suppressant effect through the hypothalamus. Phentermine also has major effects on the dopaminergic and noradrenergic nervous system, and cardiovascular effects include increased blood pressure and heart rate.[32]

Compared to the other available agents, phentermine is indicated only for short-term treatment not exceeding 3 months. It is contraindicated in patients with pulmonary artery hypertension, history of drug or alcohol abuse or dependence, or those who are treated with monoamine oxidase inhibitors (MAO-I) in the last 14 days because of the risk of hypertensive crisis.

The recommended dose is 15-30mg once daily 2 hours before breakfast. Phentermine should not be combined with other appetite suppressants. As it is associated with elevations in blood pressure and heart rate, phentermine should be prescribed with caution in patients with hypertension or cardiac arrhythmias. Other side effects include restlessness, insomnia and xerostomia.

Conclusion

More than just a public health concern, obesity affects the pharmacological treatment of patients. Changes in the body-fat composition alter the pharmacokinetics profiles of medications, thereby potentially affecting the dosing regimens in obese populations. Therefore, doctors should be mindful in using the right body weight formula to calculate medications with weight- or body-surface-area-based recommendations. Drugs with a narrow therapeutic index should be carefully monitored in obese individuals due to variances in drug distribution and clearance. Lastly, in the management of obese patients, healthcare professionals should advocate for a healthy diet, regular exercise and weight loss programmes to reduce the risk of comorbidities. Pharmacological therapy in obesity should only be considered when weight loss in spite of lifestyle interventions is insufficient to reduce a patient's BMI.

REFERENCES

1. *Ministry of Health, Singapore. National Population Health Survey - Executive Summary on National Population Health Survey 2016/17. Available from: https://www.moh.gov.sg/docs/librariesprovider5/resources-statistics/reports/executive-summary-nphs-2016_17.pdf. Accessed 26 Feb 2019.*
2. *Smit C, De Hoogd S, Bruggemann RJM, et al. Obesity and drug pharmacology: a reivew of influence of obesity on pharmacokinetics and pharmacodynamics parameters. Expert Opin Drug Metab Toxicol. 2018;14(3):275-285.*
3. *Hanley MJ, Abernethy DR, Greenblatt DJ. Effect of obesity on the pharmacokinetics of drugs in humans. Clin pharmacokinet. 2010;49(2):71-87.*
4. *Blouin RA, Warren GW. Pharmacokinetic Considerations in Obesity. Journal of Pharmaceuticcal Sciences. 1999;88(1):2-7.*
5. *World Health Organisation. Obesity. Available from: https://www.who.int/topics/obesity/en/. Accessed Feb 26 2019.*
6. *WHO Expert Consultation. Appropriate body-mass index for Asian population and its implication for policy and intervention strategies. Lancet. 2004;363(9403):157-163.*
7. *Lee YS, Biddle S, Chan MF, et al. Health Promotion Board - Ministry of Health Clinical Practice guidelines: Obesity. Singapore Med J. 2016;57(6):292-300.*
8. *NHLBI Obesity Education Initiative. The Practical Guide: identification, evaluation, and treatment of overweight and obesity in adults. Available from: https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf. Accessed Feb 26 2019.*
9. *Peymane A, Pallan M, Whincup PH. Is BMI the best measure of obesity? BMJ. 2018;360:k1274.*
10. *Casati A, Putzu M. Anesthesia in the obese patient: pharmacokinetic considerations. Journal of Clinical Anesthesia. 2005;17(2):134-145.*
11. *Chagnac A, Weinstein T, Korzets A, et al. Glomerular hemodynamics in severe obesity. American Journal of Physiology-Renal Physiology. 2000;278(5):F817-F822.*
12. *Eknoyan G. Obesity, diabetes, and chronic kidney disease. Current diabetes reports. 2007;7(6):449.*
13. *Demirovic JA, Pai AB, Pai MP. Estimation of creatinine clearance in morbidly obese patients. American Journal of Health-System Pharmacy. 2009;66(7):642-648.*
14. *Verhave JC, Fesler P, Ribstein J, et al. Estimation of renal function in subjects with normal serum creatinine levels: influence of age and body mass index. American Journal of Kidney Diseases. 2005;46(2):233-241.*
15. *Wurtz R, Itokazu G, Rodvold K. Antimicrobial dosing in obese patients. Clin Infect Dis. 1997;25(1):112-118.*
16. *Medico C J, Walsh P. Pharmacotherapy in the critically ill obese patient. Crit Care Clin. 2010;26(4):679-688.*
17. *Pai MP, Bearden DT. Antimicrobial Dosing Considerations in Obese Adult Patients. Pharmacotherapy. 2007;27(8):1081-1091.*
18. *Janson B, Thursky K. Dosing of antibiotics in obesity. Curr Opin Infect Dis. 2012;25(6):634-649.*
19. *Amstein JR, Slain D. Antifungal Dosing in Obesity: A Review of the Literature. Curr Fungal Infect Rep. 2011;5:83–91.*
20. *Koselke E, Kraft S, Smith J, et al. Evaluation of the effect of obesity on voriconazole serum concentrations. J Antimicrob Chemother. 2012;67(12):2957-2962.*
21. *Freeman AL, Pendleton RC, Rondina MT. Prevention of venous thromboembolism in obesity. Expert Rev Cardiovasc Ther. 2010;8(12):1711-1721.*
22. *Rondina MT, Wheeler M, Rodgers GM, et al. Weight-based dosing of enoxaparin for VTE prophylaxis in morbidly obese, medically-Ill patients. Thromb Res. 2010;125(3):220-223.*
23. *Thomson P, Brocklebank C, Semchuk W. Treatment dosing of low-molecular-weight heparins and the dose cap dilemma: considerations for patients in Canada. Can J Hosp Pharm. 2009;62(5):367-374.*
24. *Myzienski AE, Lutz MF, Smythe MA. Unfractionated heparin dosing for venous thromboembolism in morbidly obese patients: case report and review of the literature. Pharmacotherapy. 2010;30(3):324.*
25. *Abernethy DR, Greenblatt DJ. Phenytoin disposition in obesity. Determination of loading dose. Arch Neurol. 1985;42(5):468-471.*
26. *Kuranari M, Chiba S, Ashikari Y, et al. Clearance of phenytoin and valproic acid is affected by a small body weight reduction in an epileptic obese patient: a case study. J Clin Pharm Ther. 1996;21(2):83-87.*
27. *Erstad BL. Dosing of medications in morbidly obese patients in the intensive care unit setting. Intensive Care Med. 2004;30(1):18-32.*
28. *Suemaru K, Kawasaki H, Yasuhara K, et al. Steady-state serum concentrations of carbamazepine and valproic acid in obese and lean patients with epilepsy. Acta Med Okayama. 1998;52(3):139-142.*
29. *Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2015;100(2):342-362.*
30. *Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. NEJM. 2016;375(4):311-322.*
31. *Saxenda® product insert, Novo Nordisk A/S, Denmark 2017. Accessed 12 March 2019.*
32. *Duromine® product insert, Inova pharmaceuticals 2018. Accessed 12 March 2019.*

***MS NYX CHONG** is an outpatient pharmacist in the Department of Pharmacy, Tan Tock Seng Hospital.*

RADIOLOGY QUIZ

An 88-year-old Chinese female, premorbidly activities of daily living (ADL)-assisted and wheelchair bound, presented to the emergency department with right shoulder pain and swelling. The pain had been present for the past 6 months but worsened in the 1 week prior to presentation, with severe restriction of movement. There was no history of fall or trauma, no fever or chills. The patient has a history of pseudogout which was diagnosed many years ago.

On examination, the patient's right shoulder was swollen with tenderness on palpation. The range of motion of the right shoulder was significantly reduced due to pain. There was no local rise in temperature.

Investigations:

- WCC 12.7, HB 11.5 (microcytosis, MCV 75, MCH 26)
- INR 1.3, PT 16.4, APTT 37.3
- Na 130, K 4.2, CR 54, Urea 4.9
- CRP 2.2, ESR 31
- Blood culture: No bacterial growth

Joint fluid aspirate from the right shoulder was heavily blood stained and showed a non-inflammatory cell count. Gram stain was negative and no growth was seen on fluid culture. No crystals were seen on polarised light microscopy.

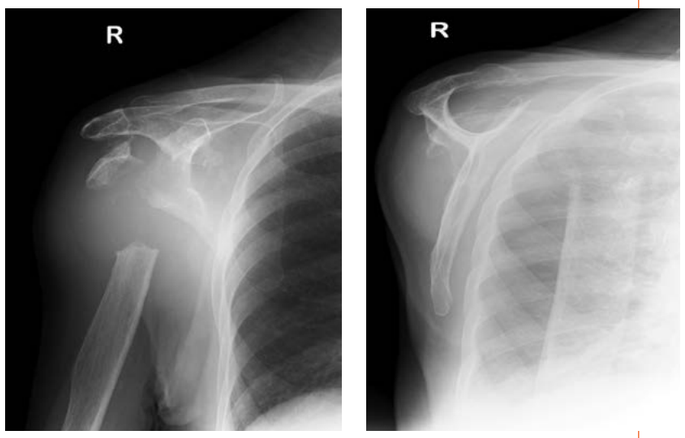


Figure 1. X-Ray of right shoulder.

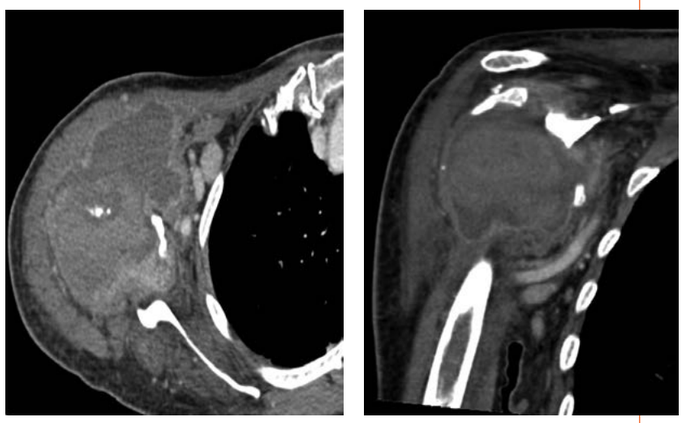


Figure 2. Contrast enhanced CT of the right shoulder.

QUESTIONS

1) What are the findings on this patient's right shoulder X-Ray?
2) What additional information does this CT provide?
3) What are the differential diagnoses for this patient's condition?

ANSWERS

1) There is complete resorption of the right humeral head and neck along with soft tissue swelling and anterior dislocation of the humeral shaft. There is also erosion of the glenoid fossa.

2) The head and neck of the right humerus is essentially replaced by a complex cystic mass, probably chronic synovitis. A large joint effusion is seen. There is also peri-articular calcifications and atrophy of the rotator cuff muscles.

3) Crystal associated arthropathy such as Milwaukee shoulder syndrome and pseudogout will be the top differential diagnosis for this case. Septic arthritis is also an important differential. However, this usually exhibits an inflammatory

synovial fluid. A Charcot joint can also have similar appearances on imaging. However, this condition is usually painless and the weight bearing joints such as the foot and ankle are more commonly affected than the shoulder. A primary (i.e. synovial) or metastatic tumour are also important differentials that need to be excluded.

The diagnosis of Milwaukee shoulder syndrome (MSS) was established. The patient was treated with oral analgesia (paracetamol, gabapentin, tramadol) and prednisolone, with symptomatic benefit.

Discussion

MSS is a rare destructive shoulder arthropathy due to intra-articular calcium hydroxyapatite deposition. It commonly affects elderly patients, typically aged 60–90 years. It has a female preponderance with the ratio of 4:1. The symptoms tend to come on insidiously, typically over months or years. Unilateral shoulder joint involvement is more common and is usually seen on the dominant side. If bilateral shoulders are involved, the disease is more advanced on the dominant side.

MSS is associated with large joint effusion and rotator cuff defects (usually completely destroyed). The hallmark of the disease is destructive shoulder arthropathy, rotator cuff loss and large recurrent joint effusions.

Patients typically present with joint pain and tenderness. The joint deformity tends to be far worse than the degree of pain experienced. The range of motion in the affected shoulder will also be restricted. Swelling due to an effusion is seen in most of the cases.

The risk factors for MSS include trauma or overuse, calcium pyrophosphate dehydrate crystal deposition (pseudogout), neuroarthropathy, female gender, and advanced age.

The pathophysiology of MSS is thought to be due to the development of calcium hydroxyapatite crystals in degenerative cartilage and in altered synovium, which are then released into the joint. These crystals, phagocytosed by synovial cells, then stimulate the release of collagenase and active protease. The release of these proteolytic enzymes results in joint and rotator cuff destruction with further release of additional crystals into the joint, thereby creating a vicious cycle and aggravating the destructive process.

Synovial fluid analysis of the affected shoulder will typically yield a haemorrhagic fluid that exhibits non-inflammatory cell count. Calcium hydroxyapatite crystals are not visible under plain or polarised light microscopy, but may be visualised by staining with Alizarin red.

X-Ray of the shoulder shows joint space narrowing, destruction of subchondral bone with bony collapse of the humeral head, soft tissue swelling, intra-articular loose bodies, and cranial subluxation of the humeral head due to rotator cuff rupture. Intra- and peri-articular calcifications usually in the supraspinatus tendon or subacromial bursa can also be seen. CT findings will be similar to radiographic characteristics. MRI may demonstrate a large joint effusion, tear of the rotator cuff as well as thinning of the cartilage and destruction of the subchondral bone.

Treatment is mainly supportive with analgesia and intra-articular glucocorticoids principally. Rest and splinting of the affected joint are also helpful.

Learning points

- Milwaukee shoulder syndrome is a rare and destructive form of arthropathy that mainly affects elderly women.
- It is characterised by intra-articular or peri-articular hydroxyapatite crystals and rapid destruction of the rotator cuff and the glenohumeral joint.
- Synovial fluid Alizarin red staining may help confirm the diagnosis of Milwaukee shoulder syndrome.

Further reading

1. *Dewachter L, Aerts P, Crevits I, et al. Milwaukee shoulder syndrome. J Belg Soc Radiol. 2012;95(4):243–244.*
2. *McCarty DJ. Milwaukee shoulder syndrome. Trans Am Clin Climatol Assoc. 1991;102:271-284.*
3. *Soares I, Mewar D. Milwaukee Shoulder Syndrome – an incidental finding but important cause of acute shoulder arthropathy. Rheumatol Adv Pract. 2017;1(1):rkx011.005.*
4. *Santiago T, Coutinho M, Malcata A, et al. Milwaukee shoulder (and knee) syndrome. Case Reports 2014;2014:bcr2013202183.*
5. *Llauger J, Palmer J, Rosón N, et al. Nonseptic monoarthritis: imaging features with clinical and histopathologic correlation. Radiographics. 2000;20 Spec No:S263-78.*

DR SURENDRAN RAJENDRAN
is a resident in the Department of Diagnostic Radiology, Tan Tock Seng Hospital.

ECG QUIZ

An elderly gentleman with history of hypertension lost consciousness for a few minutes when walking along the street. He was brought to a nearby general practitioner, who tended to him and then summoned the ambulance. At the hospital emergency department, he was fully conscious with no other complaints. A resting 12-lead electrocardiogram (ECG) was performed (Figure 1).

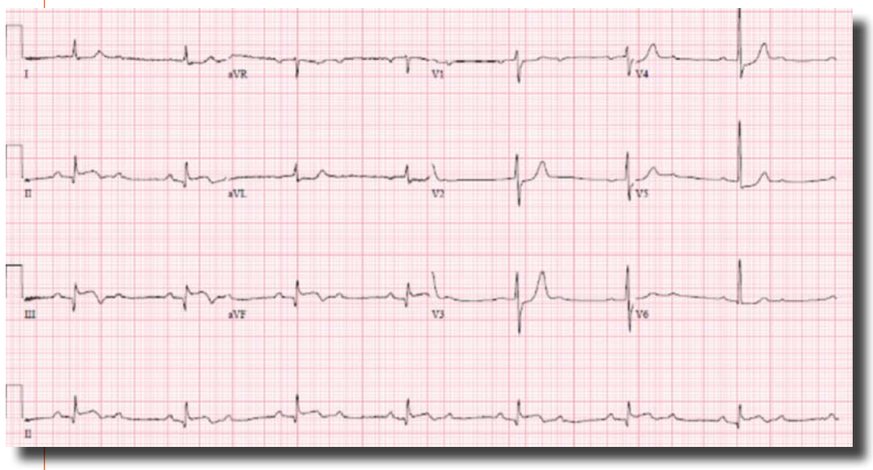


Figure 1. 12-lead ECG of an elderly man who briefly lost consciousness.

QUESTIONS

1. Based on the ECG alone, what is the most likely cause for his sudden loss of consciousness?
2. What is the next management step?

ANSWERS

1. Bradyarrhythmia (Complete heart block) secondary to an inferior ST elevation myocardial infarction (STEMI).
2. Urgent coronary angiography and percutaneous coronary intervention (PCI).

Discussion

Atypical presentation of STEMI may occur, especially in the elderly. The ECG in figure 1 shows ST elevation in the inferior leads (II, III, aVF) with reciprocal ST depression in I and aVL, consistent with inferior STEMI. There is bradycardia of 44/min. The loss of relationship between the P waves and QRS complexes is consistent with complete atrioventricular (AV) block. Although other complications of myocardial infarction (such as a self-aborting ventricular arrhythmia) cannot be excluded, the most obvious cause for his syncope appears to be bradyarrhythmia. Urgent cardiac catheterisation showed a completely occluded right coronary artery (RCA). He reverted to sinus rhythm after successful PCI and did not require cardiac pacing.

The inferior/posterior wall of the heart is supplied by a branch of the right coronary artery (RCA), the posterior descending artery, most of the time. Similarly, the AV node also receives blood supply from the RCA in most people. Acute occlusion of the RCA can result in ischaemia of the AV node, resulting in AV nodal block. In some individuals however, the posterior descending artery arises from the left circumflex artery (LCx) in what is known as a left dominant circulation. Because of this normal anatomical variation, an inferior STEMI can be due to either RCA or LCx occlusion. Classically, the RCA (rather than the LCx) is the culprit vessel when the degree of ST segment elevation in lead III exceeds that in lead II, as demonstrated in the above ECG. This information is very useful to the cardiac interventionist for planning the approach for urgent coronary angiography.

Given the pathophysiology of AV block in the setting of inferior STEMIs, the mainstay of treatment is to urgently restore coronary perfusion to the culprit vessel and AV node. In practice, AV block resolves rapidly after reperfusion and cardiac pacing is seldom required. In contrast, high grade heart blocks occurring in the setting of anterior STEMIs indicate extensive infarction and a poor prognosis.

References

1. *O'Gara PT, Kusghner FG, Ascheim DD, et al. 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. Circulation 2013;127:e362-425.*
2. *Verouden NJ, Barwaru K, Koch KT, et al. Distinguishing the right coronary artery from the left circumflex coronary artery as the infarct-related artery in patients undergoing primary percutaneous coronary intervention for acute inferior myocardial infarction. Europace 2009;11:1517-1521.*

DR YEW MIN SEN
is a consultant in the Department of Cardiology, Tan Tock Seng Hospital.