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DOCTORS TELL DOCTORS 'Get your flu shot'[1]

"The best way to motivate patients to have the flu vaccine is to have the flu vaccine yourself"[2]

Dr George Kassianos, Royal College of General Practitioners, UK Immunisation Lead

Dr Kassianos shares a few insights as to how to encourage your patients to have their flu vaccine.

Healthcare provider recommendation remains one of the most critical factors influencing vaccination[3]

On the back of the COVID-19 pandemic, and potential co-circulation of Influenza and SARS-CoV-2, your role has become even more critical to ensure:[4]

- Differential diagnosis in patients with respiratory illness[5]
- Optimal control of Influenza in high-risk groups[4]
- Decreased burden on healthcare systems[4]
- Reduced absenteeism among health workers (greater risk of exposure than general population)[4,6]

A US survey among healthcare workers during the 2014-2015 Influenza season found:[7]

Reported Influenza-like illness[7]

Reported working during their illness for a median duration of 3 days[7]

Besides the risk to your health, and possible negative impacts on patient care, you risk infecting vulnerable patients, potentially contributing to increased mortality as a result of Influenza.[6]

The NICD and WHO recommend that ALL healthcare workers are vaccinated against seasonal Influenza[6,8]

Doctors can be excellent role models to their patients, their peers, families and communities by getting vaccinated against Influenza[1]

Based on your recommendation, patients are **3 x more likely** to get vaccinated[3]

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GET A GRIP ON FLU THIS SEASON

References: **1**. Finnegan G. Vaccines Today. DOCTORS TELL DOCTORS 'GET YOUR FLU SHOT'. Available from: https://www.vaccinestoday.eu/stories/doctors-tell-doctors-get-your-flu-shot/. Accessed date: 5 October 2021. **2**. Vaccines Today. FAMILY DOCTORS ARE KEY TO PROTECTING AGAINST FLU. Available from: https://www.vaccinestoday.eu/stories/family-doctors-are-key-to-protecting-against-flu/. Accessed date: 11 October 2021. **3**. Henninger ML, Irving SA, Thompson M, *et al.* Factors Associated with Season Influenza Vaccination in Pregnant Women. *J Women Health* 2015;24(5):394-402. **4**. WHO SAGE Seasonal Influenza Vaccination Recommendations during the COVID-19 Pandemic. Interim guidance, 21 September 2020. Available from: https://www.who.int/immunization/policy/position_papers/Interim_SAGE_influenza_vaccination_recommendations.pdf. Accessed date: 30 September 2021. **5**. NICD Seasonal Diseases. Influenza 2021. *Communicable Diseases Communiqué*, October 2021;20(10). Available from: https://www.nicd.ac.za/scientific-publications/. Accessed date: 3 November 2021. **6**. Chiu S, Black CL, Yue X, *et al.* Working with influenza-like illness: Presenteeism among US health care personnel during the 2014-2015 influenza season. *Am J Infect Control* 2017;45(11):1254-1258. **7**. WHO Europe. Fact sheet for health care workers: Protect yourself and your patients from influenza. Available from: https://www.euro.who.int/en/health-topics/communicable-diseases/influenza/news/news/2014/10/influenza-common-questions-answered/fact-sheet-for-health-care-workers-protect-yourself-and-your-patients-from-influenza. Accessed date: 12 October 2021. **8**. Blumberg L, Cohen C, Dawood H, *et al.* Influenza. NICD recommendations for the diagnosis, management, prevention and public health response. Version 1.4 (12 April 2021). Available from: https://www.nicd.ac.za/wp-content/uploads/2021/07/Influenza-guidelines_-April-2021-final.pdf. Accessed date:30 September 2021.

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SAPJ Author Guidelines

Thank you for choosing SAPJ in which to publish your paper.

Aims, scope and review policy

SAPJ is aimed at the continuing professional development of the South African pharmacist in a variety of practice settings, including clinical pharmaceutical care practitioners in a community or hospital pharmacy environment, and pharmacists in academic and industrial practice.

The journal accepts specific clinical reviews on self-medication topics (symptomatic therapy) and information on prescription medication (therapy in clinical context), and provides pharmacists with essential information for referring customers for early medical attention should it be required. SAPJ further recognises that the role of the pharmacist continually evolves to meet the needs of the population. An example of this is the provision of accessible, basic primary health care services in community pharmacies.

Papers dealing with medicines safety issues, including the safe and appropriate prescription, administration and use of medication as well as pharmacovigilance, are strongly advocated in SAPJ. SAPJ further supports pharmacists in transforming the pharmacy into an accessible, basic primary health care facility for preventing and treating primary health care conditions through diagnosis, screening and treatment.

The journal is currently indexed by Google Scholar via www.sapj.co.za and enjoys wide international exposure. An 'electronic long, paper short' policy will be followed for original papers where abstracts of original papers are featured in the printed copy with the full version available online.

Online submission

All articles must now be submitted online at www.sapj.co.za

The electronic submission process will prompt you to check off the following declarations:

1. This manuscript has currently only been submitted to SAPJ and has not been published previously.
2. This work is original and all third party contributions (images, ideas and results) have been duly attributed to the originator(s).
3. Permission to publish licensed material (tables, figures, graphs) has been obtained and the letter of approval and proof of payment for royalties have been submitted as supplementary files.
4. The submitting/corresponding author is duly authorised to herewith assign copyright to Medical and Pharmaceutical Publications (Pty) Ltd
5. All co-authors have made significant contributions to the manuscript to qualify as co-authors.
6. Ethics committee approval has been obtained for original studies and is clearly stated in the methodology.
7. A conflict of interest statement has been included where appropriate.
8. A title page has been uploaded as a separate supplementary file and the submission adheres to the instructions to authors in terms of all technical aspects of the manuscript.

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Article sections and length

The following contributions are accepted (word counts include abstracts, tables and references):

Original research:	3 200–4 000 words
Evidence- based pharmacy practice:	3 200–4 000 words
Reviews:	2 400–3 200 words
Case studies:	1 800 words
Scientific letters:	1 200–1 800 words
Letters to the editor:	400–800 words

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A Piece of my Mind

Editorial Comment

SAAHIP news

The recent SAAHIP conference dominates the news in the SAPJ this month. It's no secret that I am still privileged enough to be involved with SAAHIP. I still find it amazing that the SAAHIP branches achieve so much for their members without any secretariat support. What makes these pharmacists so motivated? Where do they find the time, and especially the energy, to fit in voluntary association work in between family and employment commitments?

I do need to tease the SAAHIP secretary, however. He states in the conference report that, at the SAAHIP quiz night, "The category that really separated the men from the boys was SAAHIP's history." Obey, I feel a punishment coming on for you for this discrimination against the women who participated – they were already separated from the boys. (Your punishment involves grapefruit tonic – I look forward to it!)

YPG news

As mentioned in the last issue, our young pharmacists feature prominently throughout the country, and so they should. Their pilot mentorship programme last year was a great success and it's good to see it going ahead again this year. It does occur to me, however, that even if we are not officially enrolled in a mentorship programme, we are really all honour bound to nurture young pharmacists whenever the opportunity presents itself. Nothing annoys me more than hearing of older pharmacists who discourage the younger ones by their negativity. Yes, we have to be realistic about our challenges, but there are pharmacists who are great role models and who, against all odds, achieve both professional and personal goals – it's not impossible.

The accidental pharmacist

Take Sham Moodley as an example! I really empathised with his becoming a pharmacist accidentally! I suspect that many of us did – often what we think we want to do when we are young would be totally wrong for us. And sometimes doors open and we just walk through them, not knowing that it will lead us to where we need to be. So Sham's career has proved that he ended up in exactly the right career at the right time!

Using a webinar as a CPD opportunity

I wonder if Cheryl Stanton is also an accidental pharmacist? Was it easy to become a pharmacist when her dad is a pharmacist? Or did she resist it at first? Whatever! I must say that I really enjoyed her reflection on the webinar on the POPI Act. She makes CPD recording seem very easy. I hope that other pharmacists are doing the same. And the webinars really provide ideal opportunities for this.

Competency standards

Cheryl also impressed me by linking her learning to a competency standard, slotting it neatly into a domain and its appropriate competency. Do you know the domains and competencies? And if not, do you know where to find them?

The grapevine tells me that the competency standards for pharmacy support personnel are about to be published for implementation. These should really make it easier to determine whether or not pharmacists are permitting (or expecting) support personnel to perform acts for which they are not trained and which fall outside their scope of practice.

Ingestible biosensors

The latest PSSA entry on Facebook intrigues me. It asks members for suggestions about digital health applications or interventions that facilitate medication adherence, including ingestible biosensors. I'm afraid that I'm at the age when an ingestible biosensor makes perfect sense, except that I suspect it would be incredibly disruptive if it went off every time I forgot to take something! I won't bore you with my shopping list of chronic medicines – it might tempt you to look for interactions – but I sometimes wonder if I shouldn't book an appointment with my local clinical pharmacist to interrogate whether or not there is really any clinical benefit in taking them at my age. There would certainly be financial benefit in NOT taking them! Oh well. In this case, I'm the patient, not the pharmacist. And as the well trained pharmacist's assistant gently told me when I took in a prescription for an acute condition a week after it was written, "You do realise that if you'd brought this in last week, you'd already be feeling much better, don't you?" I couldn't argue!

Lorraine Osman

President's Message

The times they are a' changing!

Joggie Hattingh
PSSA President

What a hectic time we are living in! COVID-19 has changed the world as we knew it, and whilst it is still in our midst, we have what threatens to become another major international war on our hands.

I'm not going to try and look into a crystal ball to predict how it will affect us, but it will certainly bring hardship to many a person walking this earth and we will not escape.

We should accept medicines availability challenges to follow for a start, but that we have become quite adept at handling. However, we should get our plans in order to manage any possible emergencies.

What can we learn from the leadership the different parties to this conflict have exhibited? Starting with Vladimir Putin's leadership, who has been described as an oppressor, tyrant, autocrat, dictator, bully, and authoritarian. I think it will suffice to say that history will not look kindly on this act of aggression perpetrated by him and the immeasurable suffering he brought to the people of Ukraine and to his own people.

On the other hand, Volodymyr Zelenskyy, the President of Ukraine, has shown us what leadership is truly about.

What does it say to us as the Pharmaceutical Society of South Africa? What about our leaders in branches, sectors and at national level? Are our leaders there to get maximum mileage out of their tenure for personal gain?

In my experience, by far, the majority of our pharmacy leaders are toiling away for the benefit of the profession in their private time and with no remuneration, for truly altruistic purposes. Their main motivation is the love of the profession! Yet just because the vast majority fall into this category does not mean there is not a single exception who is pursuing a leadership position to gain perceived power. As the members and as "general council" we need to ensure that our vote goes to the correct leader, one with a clean track record and the right intent.

As leaders, we must understand that our role is one of stewardship. In the modern era, leadership is no longer about power, it is about influence and according to Professor Edward Christian Kieswetter, this entails the following:

Leaders – the six I's of stewardship

- **Intent** – they are clear about their intentions and are resolute in achieving them.
- **Impact** – they are genuinely concerned about their impact on ALL stakeholders.
- **Insight** – they work hard to understand the issues and take nothing for granted by sharing insights.
- **Inspire** – they inspire followership—being 'inspired' literally means being 'in-spirit' or drawing from the highest, noblest sense of who they are—then energising others to follow.
- **Influence** – they accept that they must earn the trust of those who do not initially take their path. They understand that these individuals often become key supporters.
- **Interdependency** – they realise that they cannot act alone. Central to their success is their ability to mould individuals into a community of common purpose.

Please take time to ponder the profound meaning these six elements of stewardship brings to the concept of leadership!

I sincerely hope that the young leaders and equally the mature leaders in our profession will use this opportunity, where we stand in awe of a young president who showed us true leadership through his humility and his total dedication to the fate of his people, but equally as we stand in horror of another who has no regard for the death, devastation and hardship he is causing, to reflect on our own role as leaders.

Do we see ourselves as "stewards" of the profession or as the "power that be" in the profession?

We will be judged by future generations accordingly.

Why hypertonic saline?

According to medical research, hypertonic saline solutions may play a big part in eradicating viruses and bacteria that enter the body through the nose. With a higher salt quantity in the product than what is in your body, hypertonic saline is more effective at drawing fluid from the inflamed, swollen lining of the nose, sinus, larynx, and bronchi to help open your airways and thin mucus, which could help to reduce the ability of a virus to attach itself to the membranes and reduce the risk of infection.

Kuraflo saline solutions

With the ***Kuraflo Hypertonic Saline Solution*** range of products, you can choose to **nebulise**, **spray,** or **nasal rinse**. We aim to help you *breathe better* in a more natural, effective, and safe way.

Whatever the choice, Kuraflo is safe to use as a preventative product or to help treat symptoms when you are sick.

- Kuraflo **3% Nebulising Solution** will help reduce swelling in the larynx, trachea, and bronchi in conditions like croup, bronchitis, allergies, dry coughs, colds & flu, and airway irritation.
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- Kuraflo **3% Adult Spray** is for children over 12 years and adults and assist in pregnancy rhinitis, swelling from allergens or bacteria, post-nasal drip, congestion, and infection.
- Kuraflo **Nasal Rinse** can be mixed at either 1.5% or 3% and are safe for any age. Nasal rinsing is still one of the best methods for severe infections and alleviating congestion, as well as using it as a postop treatment for cleansing.

Mesh vs jet nebuliser

Nebulising has become much more common over the last couple of years. Especially since the outbreak of COVID-19, there has been a dramatic increase in nebuliser and nebulising solution demand.

Mesh nebulisers have become much more popular, and about 60% of clinical trials are done with mesh nebulisers compared to about 36% of trials done with jet nebulisers.

Jet nebulisers work with a compressor to turn liquid into a mist. They are much bulkier, generate loud noise, and need a plug point to operate, limiting portability. There is also more medication residual, and because of air circulation in the chamber, medication may be diluted towards the end of nebulisation.

Mesh nebulisers are virtually silent and have shorter treatment times since medication passes through a vibrating mesh membrane the first time and has no circulation in the medication chamber. This results in almost no residual and is, therefore, more effective.

It is portable and can be used anywhere since most are battery-operated.

Kuraflo mesh nebuliser

- Up to 7 000 laser-drilled holes (more than most mesh nebulisers) for a finer mist, better absorption into the lungs, and 4–10 minute nebulising time
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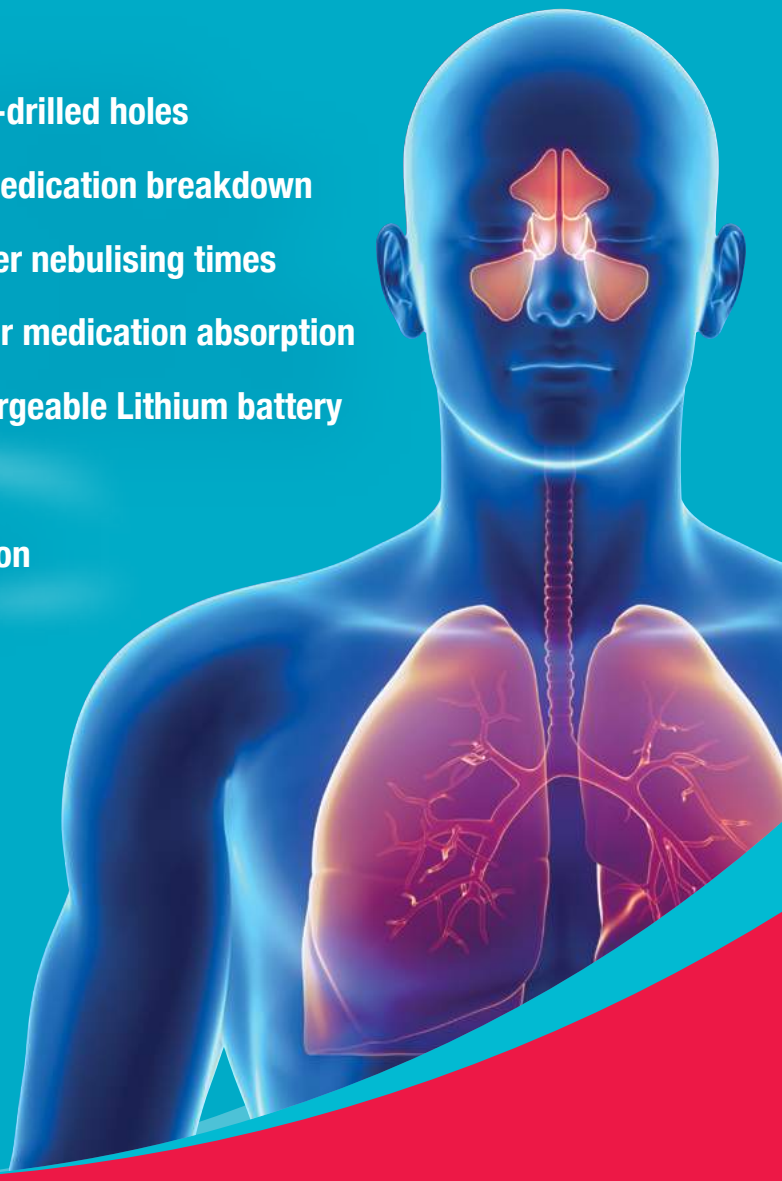

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PSSA Conference 2022

The PSSA is excited to announce that we will host an in-person conference with virtual attendance as well on 1–3 September 2022 at the Indaba Hotel and Conference Centre, Fourways, Gauteng.

Adcock Ingram OTC has partnered with the PSSA as the Gold Sponsor for the conference.

PSSA conference announcement

SAPC Stakeholders meeting

The PSSA attends SAPC Stakeholders meetings on a regular basis. The latest stakeholders meeting was held on 5 April 2022 and the issues below were raised at the meeting.

1. **Pharmacy self-inspections**

   SAPC implemented the new grading methodology, revised inspections questionnaires, self-inspections and submission of improvement plans by RPs in April 2020.

   In order to assist RPs to comply with GPP requirements and to familiarise themselves with the questions and what is expected during an inspection, RPs are required to complete a self-inspection of their pharmacy and submit it annually by 1 March. The self-inspection is submitted via the secure site on the Council's website.

   RPs are reminded to perform these self-inspections in order to avoid disciplinary actions. The SAPC has granted a grace period for the self-inspections to be completed.

2. **Pre-May 2003 pharmacies – licences**

   Pharmacies that were registered with the SAPC prior to 1 May 2003 do not have a pharmacy license from the National Department of Health (NDoH). This sometimes poses problems for the pharmacy, the SAPC and the NDoH. SAPC has resolved that all pharmacies registered prior to 2 May 2003 be required to obtain a licence from the NDoH and to record such licences with SAPC. This would be done without an application fee, provided that the pharmacy was still at the same premises as at 2 May 2003 and that ownership had not changed. The SAPC will send communication regarding this to the affected pharmacies' RP and/or owner and the RP and/or the owner should respond to this communication immediately. If there have been any changes to the ownership or the pharmacy has moved premises, the pharmacy would have to follow the normal process to apply for a licence.

3. **Pharmacies operating without responsible pharmacists (RPs)**

   Regulation 22 of the regulations relating to the practice of pharmacy states that: "Every pharmacy shall, except in such circumstances and subject to such conditions as may be published in rules by the council, be conducted under the direct personal supervision of a responsible pharmacist whose name must be displayed conspicuously over the main entrance of such pharmacy." Pharmacies where there is no RP for more than 90 days are referred for removal in terms of the Guideline for the Removal of Pharmacy Registration/ Recording as a result of non-compliance with GPP and other pharmacy legislation.

   Members are reminded that if you were the RP for a pharmacy and you resign, it is your responsibility to inform the SAPC that you have resigned as RP. This is done online on your SAPC profile.

4. **Pharmacists employed by the State but also an RP for a privately owned pharmacy**

   Regulation 22 of the regulations relating to the practice of pharmacy states that: "Every pharmacy shall, except in such circumstances and subject to such conditions as may be published in rules by the council, be conducted under the direct personal supervision of a responsible pharmacist whose name must be displayed conspicuously over the main entrance of such pharmacy." Therefore an RP is supposed to be physically present in the pharmacy during the core operating hours of the pharmacy (usually between 8 am and 5 pm). It is physically impossible for a pharmacist to be employed by the State and perform their duties in the State facility and to physically be present in a privately owned pharmacy where they are the RP at the same time.

This is considered fraud, and the SAPC will take disciplinary action against the RP.

This is also fraudulent in terms of the Public Service Regulations of 1999 (Code of Conduct for the Public Service) which regulates remunerative work outside of Public Service (RWOPS). In terms of Section C.5.5 of the Public Service Regulations (Code of Conduct), an employee may not, without approval, undertake remunerative work outside her or his official duties or use the equipment from his or her official place of employment for such work. Furthermore, RWOPS shall in no way interfere with an employee's duties for the Province/State in terms of either time or content. Permission to perform RWOPS will be considered only if the proposed employment takes place entirely outside an individual's official hours of employment for the State/Province.

5. Nurses practising in private sector pharmacies

There have been several queries from the profession for clarity on the practice of nurses in pharmacies. It has come to the attention of SAPC that several pharmacists/pharmacy personnel are dispensing nurse-generated prescriptions from their pharmacies. This practice needs to be discouraged and compliance to the legislation regarding nurse prescribing and dispensing framework should be complied with. PSSA hosted a webinar in 2020 titled "Prescribing – who may prescribe and for whom?". The recording of the webinar can be accessed on the PSSA website on the members' login platform under the legislation series.

The only concession in legislation that allows nurses to prescribe and dispense is referred to in Section 56(6) of the Nursing Act, 2005 (Act 33 of 2005):

"56(6) Despite the provisions of this Act, the said Medicines and Related Substances Act, 1965, the Pharmacy Act, 1974 (Act 53 of 1974), and the Health Professions Act, 1974 (Act 56 of 1974), a nurse who is in the service of –

a. the national department;
b. a provincial department of health;
c. a municipality; or
d. an organisation performing any health service designated by the Director-General after consultation with the South African Pharmacy Council referred to in section 2 of the Pharmacy Act, 1974, and who has been authorised by the Director-General, the head of such provincial department of health, the medical officer of health of such municipality or the medical practitioner in charge of such organisation, as the case may be, may in the course of such service perform with reference to –
    i. the physical examination of any person;
    ii. the diagnosing of any physical defect, illness, or deficiency in any person; or
    iii. the keeping of prescribed medicines and their supply, administering or prescribing on the prescribed conditions;

any act which the said Director-General, head of provincial department of health, medical officer of health or medical practitioner, as the case may be, may, after consultation with the Council, determine in general or in a particular case or in cases of a particular nature, if the services of a medical practitioner or pharmacist, as the circumstances may require, are not available."

6. Destruction of schedule 5 and 6 medicines guideline

SAHPRA published a new guideline on the destruction of Schedule 5, 6, 7 and 8 medicines at the end of 2021 (Guideline 5.05). There have been issues highlighted within the guideline that caused some concerns in practice, e.g. an application fee for the authorisation of destruction of schedule 5 and 6 medicines for community and hospital pharmacies. These issues were tabled with SAPHRA by various stakeholders.

SAHPRA explained that they require the information on the quantities of schedule 5 and 6 substances as they need to report annually to the International Narcotics Control Board (INCB) on the quantities of narcotics imported, manufactured, exported, consumed and destroyed in South Africa in order to obtain the allocated estimates for South Africa for the next year. The INCB has requirements for annual reports of scheduled substances by countries and if the numbers in South Africa are not adding up, it could affect the estimates the country is given for import and manufacturing specifically.

SAHPRA has agreed that the guideline in its current format has been retracted and will be redrafted after internal and external consultation. PSSA will inform members once an updated guideline becomes available.

SAPHEX 2022

On 6 and 7 April 2022, the South African Pharmaceutical Exhibition (SAPHEX) and The Pharmacy Show (TPS) took to Sandton Convention Centre. For the first time in more than 2 years, it was great to have the pharmacy sector coming together again and to be able to connect face to face with colleagues and friends in the industry.

The anticipation of FIP 2024 was highlighted at this year's stand with a large custom banner

PSSA and the four Sectors had a combined stand across the walkway from the TPS theatre. Representatives from all four divisions were at the stand to engage with members – existing and new – and to share information and services offered by the Society including membership application forms, professional indemnity insurance for pharmacists and pharmacy support personnel, PPS short-term insurance, Alpha Pharm distance learning programme, member benefits, sector information and other handout items. It was lovely to be able to engage with members on a personal level.

POPI Act webinar

The Cape Midlands Branch of the PSSA hosted a webinar on POPI compliance in the face of medication abuse. The presenter was Adv. Elsabé Klinck and the focus of the webinar was the effect of the POPI Act on the sharing of information between healthcare professionals when dealing with stolen or fraudulent prescriptions or patients addicted to certain medications. The Chair of the branch, Cheryl Stanton, wrote her personal reflection on the webinar and has agreed that it can be shared with other PSSA members.

POPI compliance in the face of medication abuse

Cheryl Stanton, Chair: Cape Midlands Branch of the PSSA

This is a personal reflection on a recent webinar event

Reflection on learning need

Cheryl Stanton

As a community pharmacist, medication abuse, misuse and overuse are an unfortunate reality evident in many pharmacies, including ours. Patients with an unhealthy relationship to these medications lead them to utilising different, and sometimes unlawful, avenues to procure such medication. We would sometimes receive a call from the prescriber requesting that no further medication should be dispensed for a specific patient. Sometimes it is the family of an addicted patient that appeals to our pharmacy to not dispense any medication to the patient. Often, we are informed that a prescriber's prescription pad has been stolen by a patient and to be aware of potentially fraudulent scripts. Occasionally, a member of a medical aid will phone and ask for details of a prescription dispensed on the medical aid that is for one of the dependants.

The responsibility of managing this problem is not only with me as the dispensing pharmacist but with all healthcare professionals involved in the management of that patient, including the prescriber and the manufacturer of the product. However, the implications of the POPI Act do create uncertainty as to how far healthcare professionals' responsibility in terms of managing patients' addiction to medication goes, especially when thinking of the safety of a patient.

I was curious as to how the context of the POPI Act will impact on how pharmacists should handle potential medication dependence with the patient, their family, prescriber and broader healthcare network, including how to inform other pharmacists to avoid exacerbating the problem.

I've linked this learning need to domain 5 of the competency standards[1] titled Professional and personal practice and to outcome 5.4 of continuing professional development.

Planning to achieve learning need

Because many pharmacists share the same frustrations as me, the Cape Midlands Branch decided to organise a webinar on this topic with speaker Elsabé Klinck from Elsabé Klinck & Associates. The webinar was hosted on 5 April 2022, titled *POPI compliance in the face of medication abuse*. Because it is difficult to travel at night or from one town to a neighbouring one, a virtual online event was most suitable.

Implementation of new learning

This 60-minute event consisted of a speaker's presentation as well as ample time for questions and answers from attendees. Because the speaker was briefed well in advance on exactly the scope of the POPI Act that the audience wanted information on, the presentation was to the point. As the chair of the branch, it was my privilege to act as host of the event.

Evaluation

From this learning event, I've reached the following conclusion regarding whether I may disclose information on potential abuse, misuse and overuse of medication by patients:

1. In terms of section 11 of the POPI Act,[2] as a pharmacist, I might only be able to process personal information as it complies with an obligation imposed by law on me as a professional person.
2. This obligation stems from the National Health Act[3] in section 15(1), which allows me, as a healthcare worker, access to the health records of a patient and that I may disclose such personal information to any other person (e.g. a concerned family member), healthcare professional (e.g. prescriber) or health establishment (e.g. another pharmacy) as is necessary for any legitimate purpose within the ordinary course and scope of duty where such access or disclosure is in the interest of the patient.
3. The Good Pharmacy Practice (GPP) rules[4] and code of conduct for pharmacists indicate on several occasions that as a pharmacist,[5] it is my obligation to ensure appropriate medicine use.

Although as a pharmacist, I might have an obligation imposed on myself by law to disclose certain information to others, the POPI Act indicates that only the amount of information that is adequate, relevant and not excessive should be disclosed and only for a specific, explicitly defined and lawful purpose which relates to my function or activities performed in my daily duty as a pharmacist.

It is, however, important for me to remember that should I detect potential medication abuse, misuse or overuse for any potential patient, and I want to share the information with another person, healthcare professional or health establishment, the patient implied must be informed of my intention to do so, in order to adhere to transparency.

Although my learning need is fully met after attending this event and I could apply the information in my current workplace, what could be pursued going forward is to request the South African Pharmacy Council (SAPC) to develop a code of conduct for pharmacy professionals with regard to collecting, sharing and keeping of information in terms of POPIA.

References

1. South African Pharmacy Council (SAPC). 2018. Competency Standards for Pharmacists in South Africa. Available from: https://www.mm3admin.co.za/documents/docmanager/0C43CA52-121E-4F58-B8F6-81F656F2FD17/00126360.pdf.
2. South Africa. 2013. Protection of Personal Information Act. Available from: https://www.gov.za/sites/default/files/gcis_document/201409/3706726-11act4of2013protectionofpersonalinforcorrect.pdf.
3. South Africa. 2003. National Health Act. Available from: https://www.gov.za/documents/national-health-act.
4. South African Pharmacy Council. 2004. Good pharmacy practice rules. Available from: . https://www.pharmcouncil.co.za/Media/Default/Documents/Rules%20published%20in%20terms%20of%20section%2035A%20of%20the%20Pharmacy%20Act%2053%20of%201974.pdf.
5. South African Pharmacy Council. 2008. Rules relating to the code of conduct. Available from: https://www.pharmcouncil.co.za/Media/Default/Documents/Rules%20published%20in%20terms%20of%20section%2035A%20of%20the%20Pharmacy%20Act%2053%20of%201974.pdf.

The PSSA/Alpha Pharm distance learning programme 2022

The PSSA/Alpha Pharm distance learning programme continues to offer pharmacists useful, practical, up-to-date information that enables them to provide optimal pharmaceutical care to their patients.

Module 2, 2022 – Adult vaccinations

Most people are aware of the need for infant immunisations but very few realise that there are valuable vaccines available for adults and adolescents as well. This module explains why vaccines are necessary for adults and adolescents and in various adult population groups. The pharmacist can play a key role in encouraging the uptake of the various vaccines for adults and adolescents as well as in those pharmacies that have a clinic, by providing such a service to the public.

Vaccines play a vital role throughout the circle of life protecting both the individual as well as the community – from the mother and grandparents being vaccinated to protect the newborn infant, to vaccinated babies and young children providing protection to their grandparents. And not to forget the importance of adolescents benefitting from the protection of vaccines. 25% of our South African population are adolescents and future leaders of our country, so it is important to ensure their health.

Over the years, vaccination has significantly reduced the burden of vaccine-preventable infections among infants and children. According to the WHO, 2–3 million lives are saved every year due to vaccinations. However, evidence has shown that immunity acquired through some childhood vaccinations, for example, tetanus, diphtheria and pertussis, wanes with time. As a result of waning immunity, older children, adolescents and adults become vulnerable to these infections. In the United States of America, 99% of vaccine-preventable deaths (VPDs) occur in adults. In 2006, 200 children died from VPDs whereas > 70 000 adults died from VPDs in the USA. It is therefore increasingly recognised that vaccination across all age groups (not only infants and children) is important.

This module will enable you to have all the necessary information to be able to advise people about adult and adolescent vaccinations and boosters, which ones are indicated at which stages of life and when and how they should be administered.

For more information about this programme, contact Gill or Glynis at Insight Medicine Information on 011 706 6939 or email: cpdalphapharm@insightmed.co.za.

The PSSA/Alpha Pharm clinical education programme 2022 for pharmacy staff

The PSSA/Alpha Pharm pharmacy staff clinical education programme continues to offer front-shop assistants or pharmacist's assistants up-to-date information that enables them to provide optimal pharmaceutical care to their patients. All pharmacy staff need to be familiar with the use of unscheduled medicines and should be reminded of when it is necessary to refer the patient to the pharmacist.

Module 2, 2022 – Adult vaccinations

It is becoming increasingly important for teenagers and adults to be vaccinated or receive boosters because there is a weakening of protection from some vaccines given during childhood.

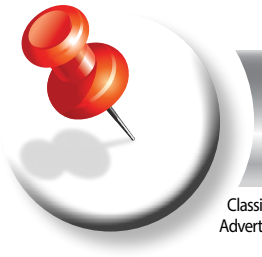
Vaccines play a very important role throughout life, starting from before the baby is even born, right up to the elderly. In some cases, vaccinating one group of people helps to protect another group. For example, some vaccines are given to pregnant women to protect the babies and vaccinating young children can indirectly protect the elderly.

Throughout the world, vaccination has played an important role in improving the health of children, especially those under the age of five years. Unfortunately, the protection provided by some vaccines given in childhood is not long-lasting and gets weaker with age. This has resulted in many more infections occurring in adults, especially the elderly. A study has shown that in the United States of America in 2006, 200 children died from infections that could have been prevented by vaccination, while more than 70 000 adults died from these infections.

South Africans are very fortunate to have access to many vaccines that can help to prevent diseases. Unfortunately, most of these vaccines are not yet widely used by adults and adolescents as the importance of them is not really understood by the public. Most people accept that babies and young children should have vaccines but then don't think about them after that. Vaccine-preventable diseases can occur at any stage of life and can be more serious in adults and the elderly.

Front-shop healthcare workers have the ideal opportunity to discuss the value of vaccines with their customers as they are often the first point of contact with customers. This module explains which vaccinations are important to have during adolescence, pregnancy and adulthood, as well as which special groups of people should be protected by having the appropriate vaccinations.

If you would like to participate in the PSSA/Alpha Pharm pharmacy staff clinical education programme, please contact Gill or Glynis for further information on 011 706 6939 or email: cpdalphapharm@insightmed.co.za.



Classifieds

Classified advertisements may be-mailed to sandy@medpharm.co.za. The placement of classified advertisements is offered as a free service to members and subscribers. Advertisements will be placed for three consecutive months, if space is available. Advertisements longer than 30 words will be edited.

Launch of the Mentorship Programme: words of wisdom from a YPG leader

Hilton Tommy Stevens
PSSA YPG

Hilton Tommy Stevens

Understanding the needs, cultures and perceptions of the different generations has been the focus of many product and service providers. Please note that my reference to "Generation" is by no means referring to the legendary Mfundi Vundlas productions, but rather to the Greatest Generation (born between 1901–1927), the Silent Generation (born between 1928–1945), Baby Boomers (born between 1946–1964), Generation X (born between 1965–1980), Millennials (born between 1981–1995) and Generation Z (born between 1996–2010). Across the spectrum of these generations, the most common phrase used during a sales pitch is: "serves more than one purpose/all purpose…". Without sounding clichéd, this represents the golden phrase for this pitch – the PSSA Mentorship Programme aims to achieve numerous objectives, across all the generations of the PSSA.

There has been a trend across many professional industries towards emphasising the need for mentorship programmes. In the 2021 Business Wire, an online publication, data from mentorship software was featured, which reflected that mentorship programmes were trending as they:

i. kept the virtual workforce engaged and productive,
ii. created dialogues across different races, and
iii. improved employee retention as much as 75% in Fortune 500 companies.

These programmes may be found in various schools, workplaces, occupations, and groups. They can operate through either structured formal programmes or less formalised platforms. Using the former approach, the PSSA's YPG has created an initiative that will achieve the following:

Provide future leaders for the PSSA

In a presentation by Raytheon Professional Services, they state that "Learning leaders from effective organisations list coaching programmes and mentor networks as a best practice for onboarding twice as often as those from ineffective organisations." The Society has continuously boasted influential leaders across all its sectors and branches. Factors contributing to this include the establishment of infrastructures for leadership development, such as pharmacy student associations at universities. Another suitable example of this is the well-established South African Pharmaceutical Students' Federation (SAPSF), and now the PSSA's YPG Mentorship Programme, which will ensure that the leadership culture is deeply rooted within the Society and the profession.

As mentioned above, the Society boasts a wealthy pool of expertise, skills, and insight concerning the responsibilities of the different roles in the pharmacy profession. These expand into the history of the profession and the different milestones achieved, such as challenges and victories that have shaped the profession into what it is today. However, as well as this concept is packaged, these types of packages exist in isolated well-packaged hubs, like the Avengers characters in their separate respectable Marvel movies. Their optimal effects can only be experienced if these packages feed off, and supplement each other's (even Iron man could not defeat Thanos alone, and only stood a chance with the rest of the Avengers). One of the objectives, therefore, through this YPG-led initiative, is to ensure the development and maintenance of a platform that will encourage engagement across the different generations. Ultimately, it is hoped that this will bridge the identified gaps.

Its benefit

Anamaria's first line in the film Pirates of the Caribbean: The Curse of the Black Pearl is an angry response to Jack, who is trying to rally up a crew. She asks, **"What's the benefit for us?"**. The benefit in the story ends up being a beautiful ship. The "what's in it for us?/ what's the benefit for us?" is a common, and relevant question the Society's members are faced with when recruiting new members.

The YPG Mentorship Programme is a new added benefit, which is available to everyone, young and old, across all sectors and branches, regardless of their position in the profession.

Evolve

One of the buzzing keywords that arose from the COVID-19 era was and is *Change*. We want to ensure, through the YPG Mentorship Programme, that all who join the Society experience both personal and professional growth. The Society's main asset is its members, and therefore its growth has a direct correlation to that of its individual members' growth. The PSSA Mentorship Programme will ensure both personal and professional growth and, more importantly, a sustainable culture/mentality of *Mentoring*.

History

If you have ever had the pleasure of attending a PSSA conference or one of its sector's conferences, you would note a common theme that exists in them, the Society's history. The history of the Society can be seen and heard subtly everywhere, whether it be through conversations during lunch and tea breaks, symbols on the medallions that are proudly worn by sector leaders, or the various features in its reputable magazines. History demonstrates a product or service's initial values, purpose and principles. One of the best ways to transfer this history and insight is through direct involvement within the PSSA, on a relatable and relevant platform – a gateway. This is the Mentorship Programme.

All purpose

Ultimately, we want to achieve what we've learned from Maslow's hierarchy of needs. We want to grow professionally in our careers and in our personal lives as well as become influential in the spaces we find ourselves in. Anshul Kapoor, author of Firsters and Fall, defines ambition as, "A strong desire to grow or achieve something and is considered a very natural human feature, arguably even a human instinct. We, however, need the tools to assist us in reaching these achievable goals." The profession needs to ensure its future, so that its history, expertise and influence in healthcare can continue to expand from strength to strength. The PSSA Mentorship Programme is the foundation that will host all these factors, creating the ultimate all-purpose product, which will cater to the needs of everyone within the Society and the profession.

PSSA Young Pharmacists' Group

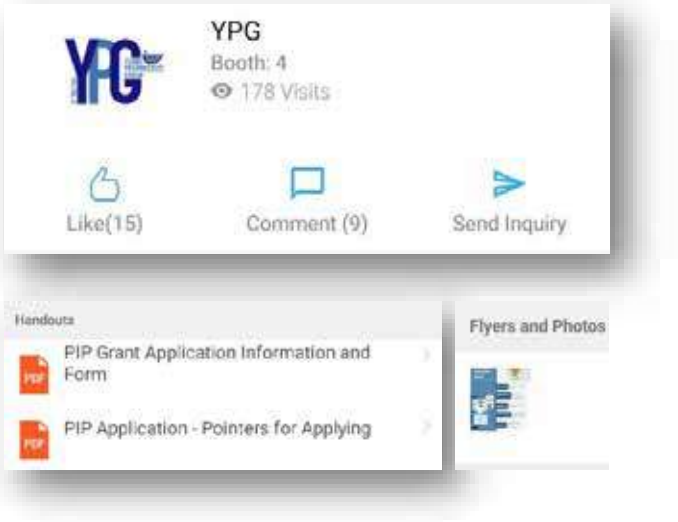
YPG presence at the first virtual SAAHIP Conference!

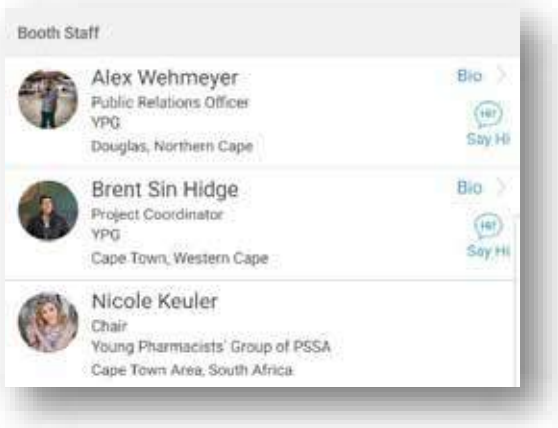
YPG's virtual booth

PSSA YPG was graciously invited to establish a virtual exhibition booth at the 2022 SAAHIP Conference in March 2022 via the Whova app.

The virtual booth provided an ideal platform for attendees to learn about YPG, its goals, projects and avenues for participation and engagement within the Society.

The interactive nature of the virtual stand enabled attendees to access various YPG-related materials and interact with other attendees.





The YPG giveaway

YPG invited all conference attendees to take part in a virtual giveaway, where they were asked to:

- Visit and like the YPG virtual exhibition stand
- Write a joke that *only a pharmacist* could understand

The specially selected YPG judges had the final vote for the best joke.

Congratulations to Armand Algra for the winning joke!

"A doctor is giving a talk at a symposium. Like any good public speaker, he wrote his speech out on notecards. Unfortunately, when he gets up to the podium, he finds that he just can't read his notes. So he says to the audience,

"Is there a pharmacist in the house?"

Feel free to reach out to us at ypg@pssa.org.za or via Facebook: Young Pharmacists' Group of PSSA

Let's walk this journey together!

Emergency contraception for the South African healthcare professional

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Introduction

Unintended pregnancies are very common, and it is estimated that almost 45% of all pregnancies in 2011 in the USA were not planned.[1] In South Africa, the situation could even be worse as it is common knowledge that we have a very high teenage pregnancy rate. It puts the already overburdened health system under enormous pressure. The social and financial pressure of an unintended or even unwanted pregnancy can be devastating to a family and even more so to a single mother. It has been reported that the unintended pregnancy rate in Botswana is 52% and that only 22% had ever used emergency contraception (EC).[2]

Although EC is widely available in the public and private sectors, women are unaware of the options available to them. A study published in 2012 reported that only 50% of female university students had heard about EC.[3] In rural populations, this number is even lower as it was previously estimated to be only 17%.[4]

What is even more concerning is that knowledge of EC amongst pharmacists and doctors is lacking. In Durban, KwaZulu-Natal, only 28% of doctors and 32% of pharmacists could correctly prescribe the Yuzpe regimen. The recognition of side-effects was even worse as only 27% of doctors and 22% of pharmacists could accurately diagnose or identify them.[5]

One can therefore expect that this lack of knowledge could lead to unsafe terminations of pregnancy and unnecessary maternal deaths. Unfortunately, at the population level, the use of EC has not reduced abortion rates, although the use of EC could be beneficial for individual women.[6]

Indications for the use of emergency contraception

What are the indications for EC?

- Contraception failure (condom that slipped or broke, missed pills, the concomitant use of enzyme-inducing drugs or antibiotics in women using hormonal contraception or an expelled IUCD).
- Sexual assault.
- Sexual coercion.
- Unprotected consensual intercourse.[1]

Emergency contraception options available in South Africa

EC can be divided into oral EC pills and copper-containing intrauterine contraceptive devices (IUCDs). The oral EC pills are:

- Yuzpe's method of combined oral contraceptives
- levonorgestrel (LNG)
- ulipristal acetate (UPA)

Each of these options will be discussed in greater detail. (Table I for a summary of EC options available in South Africa.)

Other options not registered for EC use will be briefly mentioned.

Yuzpe's method/regimen

Yuzpe's method is the use of 100 µg ethinylestradiol (EE) and 1 mg norgestrel (e.g. 2 Ovral® tablets) taken 12 hourly. Thus, 2 Ovral® tablets are taken stat and repeated 12 hours later. This regimen needs to be used within 72 hours of unprotected intercourse.[7] Ordinary combined oral contraceptives can also be used as long as each 12-hourly dose contains at least 100–120 µg EE and a progestin of 0.5–0.6 mg LNG or 1.0–1.2 mg norgestrel.[8]

Another option is to use Nordette® as each tablet contains 30 µg EE and 0.15 mg LNG. To attain the acquired dose, the woman thus needs to take four Nordette® tablets stat and repeat the dosage 12 hours later. Four Nordette® tablets contain 120 µg EE and 0.6 mg LNG.

The yellow pills in a Triphasil® package could also be used as each yellow pill contains 30 µg EE and 0.125 mg LNG; four pills will thus give a total dose of 120 µg EE and 0.5 mg LNG.

Of all available methods, Yuzpe's is the least effective, but it was still shown to reduce the risk of pregnancy by 74%.[9] Other studies have reported efficacy of 98–99% in preventing pregnancies.[8]

The sooner after unprotected coitus it is used, the more effective it is. This is also generally true for all methods of EC.[9]

Of all EC methods used, Yuzpe's method has the worst side-effect profile.[9] The side-effects include:

- nausea,
- vomiting in up to 20% of women (the most common side-effect),

- headache,
- changes in the menstrual cycle (delay in onset of menstruation), and
- mastalgia.

If a patient vomits within two hours after taking a dosage, that dosage needs to be repeated. Therefore, antiemetic drugs are recommended, such as prochlorperazine 5–10 mg, domperidone 10 mg or metoclopramide 10 mg, when Yuzpe's regimen is prescribed.[8,9]

The method of action whereby Yuzpe's regimen prevents pregnancy is mostly by inhibiting ovulation. There may also be effects on the functioning of the endometrium and thus preventing implantation of the embryo.[8] The cumulative effect on fertilisation, gamete transport and corpus luteum functioning is not clear, and due to ethical considerations, it is challenging to study in humans.[10]

There are almost no contraindications to the use of Yuzpe's regimen. Due to the high EE dosage, there may be a theoretical concern for the development of thromboembolic complications, but studies do not support this as the use of the EE is very brief.[9] Studies also do not report increased risks to an existing pregnancy.[9]

Oestrogens are metabolised by the CYP450 enzymes which are mostly expressed in the liver. The first step is hydroxylation to hydroxyestradiol, which in turn is catalysed by CYP1A2 and CYP3A4 with the inactive metabolites excreted into faeces and urine.[11] It is thus logical that enzyme-inducing medication might decrease the efficacy of EC. Drugs known to be enzyme-inducing include rifampicin, griseofulvin, carbamazepine, phenytoin, St John's Wort, nevirapine and efavirenz.[8,9]

Levonorgestrel

LNG as an EC is given orally in one of two dosages. It can be given as 0.75 mg 12 hourly for two doses or a single dose of 1.5 mg, which is now more commonly used – thus, two pills are taken stat.[12] LNG should be taken as soon as possible after unprotected intercourse and preferably before 72 hours have passed, although some studies report efficacy up to five days after sex.[9,12] There is no reported difference in the effectivity of the single 1.5 mg dose compared to the two doses of the 0.75 mg tablets. Norlevo® and VONEL® are available as 0.75 mg tablets or Escapelle® as a single 1.5 mg tablet.

It is generally understood that a woman's fertile period is between five days prior to and one to two days post-ovulation. LNG is thought to inhibit ovulation as progesterone and progestins delay the LH surge.[9,12] In order to be effective, it must be administered before the LH surge begins. It speaks for itself that it is less effective if given closer to ovulation.

LNG is more effective than the Yuzpe method in preventing pregnancies. LNG may prevent 85% of pregnancies,[8] compared to the 74% mentioned for Yuzpe's regimen.[9] Another comparison estimated the pregnancy rate to be 1.1% in the LNG group vs 3.2% in women employing the Yuzpe method as EC.[9] When meloxicam, which is a COX-2 inhibitor, was added to 1.5 mg LNG, follicle rupture was delayed even in the presence of an LH surge.[12] Obesity has a negative effect on the efficacy of LNG EC. With a BMI > 30 kg/m^2, there is a definite increase in the failure rate, with an odds ratio (OR) of 4.41.[9] Doubling the dose of LNG might be an option for obese women, and at present, it is being evaluated.[1]

The side-effect profile of LNG is favourable compared to that of the combined oral contraceptive pill used for Yuzpe's method. Although the most common side-effect is nausea (23%), followed by vomiting (5.6%), side-effects are much less common compared to those accompanying the Yuzpe's regimen.[9] LNG's mechanism of action predicts a delayed onset of menstruation because ovulation is delayed.

In a systemic review of 47 studies assessing the safety profile of LNG, it was reported that most side-effects were not serious. Uncommon adverse effects were anorexia, weight gain, ectopic pregnancy, ovarian cyst rupture, suicidal thoughts and even ovarian cancer.[13] It is debatable if all of these are really due to LNG EC as it is used very briefly and often as a once-off only.

Breastfeeding women should be able to use LNG as it does not contain oestrogen; oestrogen inhibits breast milk production. It might be better though to discard the breast milk for 36 hours after taking LNG as an EC pill.

There are no absolute contraindications to the use of LNG as EC, and as with combined oral contraceptives, it does not negatively affect a pre-existing pregnancy.[9] As a result, no pregnancy test or physical examination is required before taking the LNG EC pill.[1]

As ovulation is delayed by LNG, a woman can still fall pregnant if she has unprotected intercourse a few days after the use of the EC pill. It is, therefore, of utmost importance to counsel the patient on the use of barrier methods for contraception after the use of an EC pill such as LNG (Norlevo®/Escapelle®).

Ulipristal acetate

UPA (Ella®), as a second-generation antiprogestin, has antagonistic as well as partial agonistic effects on progesterone receptors, thus, it is a selective progesterone receptor modulator (SPRM).[7,15] UPA also blocks glucocorticoid receptors.[9] It has been marketed in Europe since 2009 and was approved for EC by the FDA in 2010.[7] As an EC, it is shown to be more effective than the LNG EC pill as it can prevent ovulation even after a woman had an LH surge.[12] UPA can be given up to five days after unprotected coitus. As the LH surge is suppressed and ovulation is delayed, the menstrual cycle is prolonged.[9] UPA also seems to be more effective in women with a BMI of > 30 with a failure rate of 2.6% compared to a 5.8% failure rate with LNG EC pills.[12] The most common side-effects of UPA are nausea, vomiting, headache and a prolonged cycle. Overall it is very well tolerated. There are no absolute contraindications to the use of UPA. Still, as it blocks glucocorticoid receptors, LNG is preferred in asthmatic women.[1] UPA is not an abortifacient.

There has been no difference in the ability of embryos to implant in endometrium that has been exposed to UPA compared to endometrium that has not been exposed.[1] It is taken orally as a single 30 mg dose.[8]

Copper-containing intrauterine contraceptive device

The copper-containing IUCD is regarded as the most effective of all EC options.[1,9,12,14] Studies reported a failure rate of only 0.1%.[7,14] The big drawback in using a copper-containing IUCD as EC is that a certain skill set and instrumentation are required for it to be inserted successfully. As a result, it is often overseen as EC.

The advantages of inserting a copper-containing IUCD as EC are numerous:

- It is cost effective.[10]
- It provides continuous/ongoing protection against pregnancy.[10]
- It does not have any hormonal effects and thus is not contraindicated in women with risk factors for deep venous thrombosis.
- It can be inserted up to 120 hours (five days) after unprotected intercourse.[1,9]
- Increased BMI does not affect the effectiveness of a copper-containing IUCD.[1]
- The efficacy of IUCDs is not affected by other medication such as enzyme-inducing drugs or antibiotics.
- Copper-containing IUCDs do not have an adverse effect on breast milk and may be safely used by lactating mothers.[1]

The copper-containing IUCD releases copper ions into the uterine cavity. Copper reduces sperm motility.[1] It is also known to cause an inflammatory reaction (increase in white blood cells and enzymes) in the uterine cavity, which is hostile to sperm.[1,9] If fertilisation does occur, the inflammatory response may prevent implantation.[9] There is also a change in the tubal environment. The copper-containing IUCD also prevents implantation,[10] but it is important to note that the changes in the uterine cavity do not affect a blastocyst that is already implanted, and furthermore, copper-containing IUCDs are not implicated in birth defects.[1]

Side-effects of a copper-containing IUCD include:

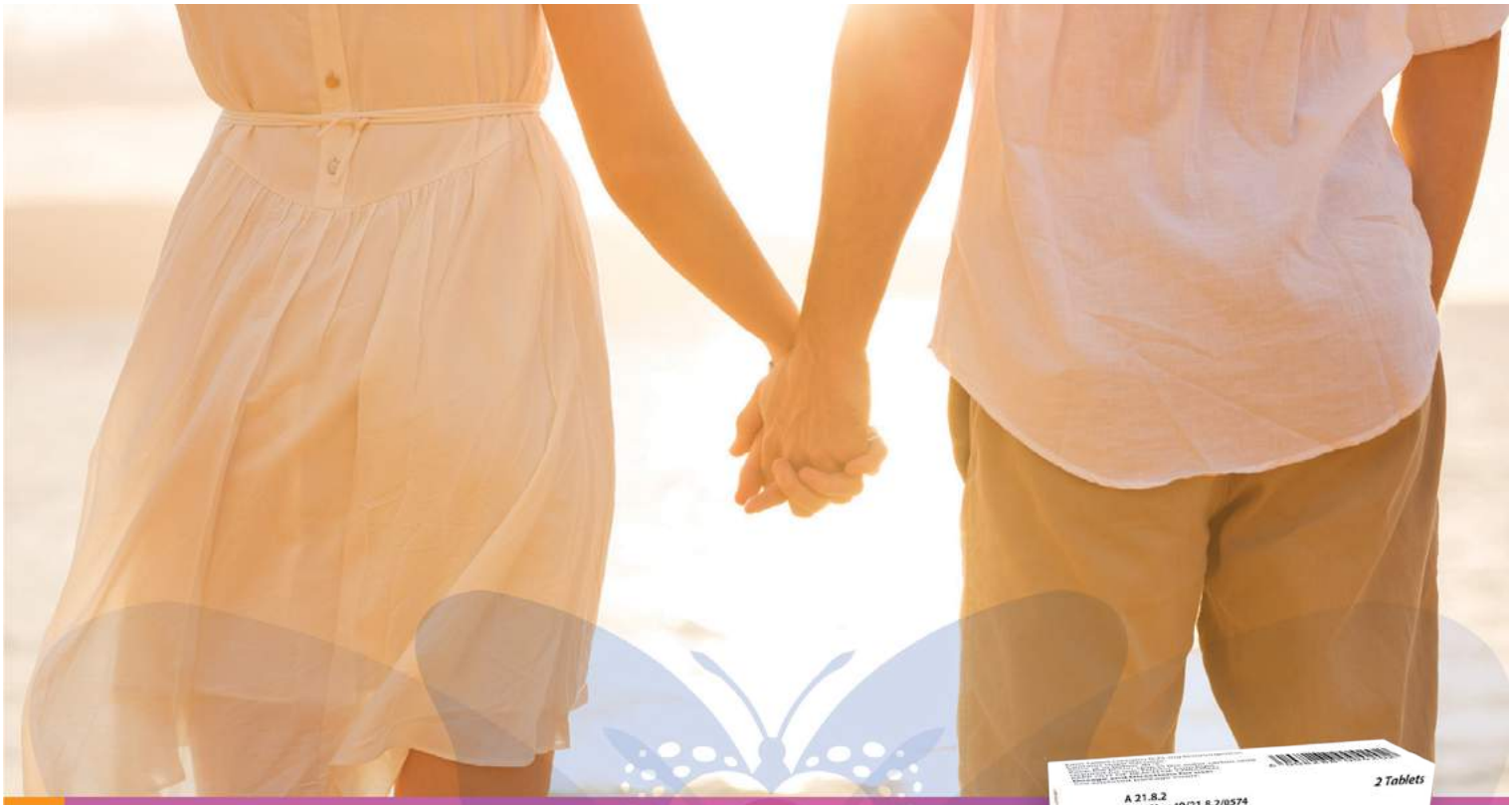
- Increased menstrual bleeding,[9] which can be managed with the use of nonsteroidal anti-inflammatory drug (NSAIDs) and tranexamic acid.
- Discomfort and pain during its insertion can be minimised with the use of local analgesia and oral pain medication such as paracetamol and NSAIDs.[9]
- There is an increase in pelvic inflammatory disease (PID) in women with a copper-containing IUCD.[10]
- The risk of malposition or uterine perforation is always present,[7] therefore, it is advisable to do a pelvic ultrasound examination to confirm the correct placement.

There are certain contraindications to the insertion of a copper-containing IUCD for EC:[1]

- Women with active PID.
- Known congenital malformation of the uterus such as duplications.
- Wilson's disease.
- Cancer of the cervix or uterus, including gestational trophoblastic disease.
- The WHO warns against the use of copper-containing IUCDs in HIV-positive women who are not using antiretroviral (ARV) therapy.

Table I: Summary of EC options available in South Africa

Method	Timing after unprotected coitus	Side-effects	Contraindications	Special considerations	Effectivity
Copper-containing IUCD Nova T 380® Single insertion	Up to 5 days (120 hours)	Pain and discomfort with insertion Increased menstrual flow	Current pregnancy Uterine abnormality PID and pelvic TB Gynaecological malignancies Abnormal uterine bleeding Wilson's disease (rare)	Training needed to insert Risk of uterine perforation	Most effective Provides ongoing contraception
LNG Norlevo®, VONEL®, Escapelle® Single dose of 1.5 mg or 2 doses of 0.75 mg 12 h apart	Within 72 hours	Nausea Vomiting Delayed menstruation	None	Less effective in obese women	Effective
Yuzpe's method Ovral® ii tabs stat and repeat after 12 h Nordette® / Triphasil® (yellow pills) iv tabs stat and repeat after 12 h	Within 72 hours	Severe nausea Vomiting Headache Mastalgia Delayed menstruation	No absolute contraindications Careful in women with known hypercoagulability	Less effective in obese women	Least effective Worst side-effect profile
Ulipristal acetate Ella® Taken as a single 30 mg dose	Up to 5 days after contraceptive failure/unprotected intercourse	Well tolerated Nausea and vomiting Headache Delayed menstruation	No absolute contraindications Careful in asthmatic patients as it blocks glucocorticoid receptors	More effective in preventing ovulation in obese women than LNG or Yuspe's method	More effective than LNG, especially in obese women



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USE RESPONSIBLY | NOT A SUBSTITUTE FOR BIRTH CONTROL

* VONEL is intended for emergencies only and is completely unsuitable for regular contraception. The reliability of VONEL is not as high as that of the contraceptive, which is taken for at least 21 days of the menstrual cycle.[1]

References: 1. VONEL tablet professional information leaflet - as approved by SAHPRA. **2.** Weismiller DG. Emergency contraception. Am Fam Physician 2004;70:707-14.

S2 Vonel 0,75 mg Tablet. Reg. No. 49/21.8.2/0574. Each tablet contains 0,75 mg levonorgestrel. Contains sugar (Lactose monohydrate 84.50 mg). PHARMACOLOGICAL CLASSIFICATION: A 21.8.2 Progesterones with or without oestrogens.
For full prescribing information please refer to the professional information leaflet approved by the South African Health Products Authority.

Applicant: Ranbaxy Pharmaceuticals (Pty) Ltd, a SUN PHARMA company. Reg. No.: 1993/003111/07.
14 Lautre Road, Stormill Ext.1, Roodepoort, Johannesburg. Tel. +27 12 643 2000. Fax. +27 12 643 2001.

Womens' Health Portfolio

SUN PHARMA

- The risk of expulsion and uterine perforation is increased if it is inserted within four to six weeks postpartum.

We have all been taught that copper-containing IUCDs increase the risk for an ectopic pregnancy, but recently it has been shown that in women not using contraception the absolute risk for an ectopic pregnancy is between 3 and 4.5 per 1 000 women years compared to 0.2 in women using copper-containing IUCDs.

Given the above, copper-containing IUCDs are still safe for the majority of women in need of EC.[14]

At present, the use of an LNG-containing intrauterine system (Mirena®) is not recommended. Currently, there are studies underway evaluating its efficacy as EC intrauterine device. Unfortunately, limited data is available.[1]

EC contraception option not registered for use in South Africa

Mifepristone

Mifepristone (RU4860, Mifegyne®) is a synthetic steroid and is an antiprogestin.[1,7,9] The mechanism of action is complex and in the follicular phase, it delays the rise in oestrogen and consequently the LH surge and therefore prevents ovulation. Once ovulation has taken place, it blocks the endometrial receptors resulting in an immature endometrium not suitable for embryo implantation.[9] In doses of 200–600 mg, it is a known abortifacient, and in this context, its use as an EC pill is controversial. Studies have shown that mifepristone has an efficacy comparable to LNG and UPA.[9]

It should be noted that, as with all other EC options that delay ovulation, mifepristone also prolongs the menstrual cycle. Other side-effects include headache and dizziness, nausea and vomiting, abdominal cramping and diarrhoea.[9] Absolute contraindications to the use of mifepristone are:[9]

- adrenal insufficiency,
- steroid therapy,
- asthma,
- porphyria, or
- hypersensitivity to prostaglandins.

Mifepristone is not registered for use in South Africa.

Ethics in emergency contraception

For EC to be a viable option, healthcare providers should be knowledgeable and non-judgemental.[16] Misconceptions abound, and often EC is seen as preventing implantation or as an abortifacient, but as seen from the discussion above, it prevents fertilisation and does not interfere with an existing pregnancy.[17,18] When seen in this context, EC pills may prevent abortion.[18]

By preventing women the right to EC pills, the ethical principles of autonomy, non-maleficence, beneficence and justice are violated.[17]

Practical considerations

EC can be obtained in private and public sectors from pharmacies and clinics without prescription.

A copper-containing IUCD is the most effective form of EC, it also provides long-term contraception.

There are no absolute contraindications to the use of LNG EC pills.

LNG EC pills are more effective than Yuzpe's method.

UPA is more effective than LNG in obese women.

All methods that delay ovulation should only be used for a single episode of unprotected intercourse.

If a woman has a second episode of unprotected intercourse in the same menstrual cycle, a copper-containing IUCD should be considered.

After taking EC pills which delay ovulation, a woman should be reminded to use additional barrier methods for contraception.

When prescribing Yuzpe's regimen, it is important to add an antiemetic drug.

The sooner EC is instituted, the lower the failure rate, i.e. less unintended/unwanted pregnancies.

EC pills should be given within 72 hours, except UPA, which can be taken up to 5 days after unprotected coitus.

A copper-containing IUCD should be inserted within five days.

Healthcare professionals working in emergency rooms and those involved with sexual assault victims should have protocols in place for the provision of EC.

It should be remembered that EC is not a long-term solution to women having unprotected sex and that long-term options should be discussed with women.

EC does not prevent sexually transmitted diseases.

If a woman's menstrual period is delayed by more than one week after her usual period should start, or if her menstruation does not commence within three weeks of taking EC pills, she should do a pregnancy test and seek medical attention.[9]

It is important to note that pregnancy should be excluded before inserting an IUCD.[10] It can be done by a urine pregnancy test, a serum β-hCG or pelvic ultrasound.

When inserting an IUCD, it is the ideal opportunity for doing a Papanicolaou smear or liquid-based cytology (LBC) of the cervix.[10]

Not one of all the methods of EC can prevent each and every pregnancy.

References

1. Haeger KO, Lamme J, Cleland K. State of emergency contraception in the US, 2018. Contracept Reprod Med. 2018;(3):20. https://doi.org/10.1186/s40834-018-0067-8.

References available on request.

Cardiac failure: an update and the role of the pharmacist

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Abstract

Heart failure (HF) often occurs in patients who have more than one comorbidity, with resultant polypharmacy. Medication errors may occur, along with adverse interactions between medicines. This highlights the importance of the pharmacist as part of the multidisciplinary team in the management of HF. Many advances have been made in the way in which heart failure is classified, diagnosed, managed and treated. The body of knowledge is ever-expanding, and hence the need for frequent review of treatment guidelines in light of the data emerging from ongoing research. This article focuses on elucidating some of the current strategies to manage and treat this condition. Certain associated pathological conditions and modalities are therefore beyond the scope of this article and the reader is advised to consult the the latest international guidelines for more detailed explanations of advanced treatment strategies, the cardiomyopathies, congenital heart defects, acute cardiac failure, and heart failure within the context of myocardial infarction, cardiac valve replacement surgery, coronary artery revascularisation and other specialised examples.

Keywords: cardiac or heart failure, cardiac output, stroke volume, ejection fraction, systolic dysfunction, LVEF, HF*p*EF, HF*r*EF, brain natriuretic peptide, NT-proBNP, ACE-inhibitor, ARB, ARNI, CCB, β-blocker

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Introduction

At its simplest level, heart failure (HF) may be defined as a complex clinical syndrome, which is caused by impaired ventricular filling or contractility, and which typically manifests itself through varying degrees of dyspnoea, fatigue and oedema. Thus, HF (*syn.* cardiac failure, or CF) refers to the inability of the heart to meet the metabolic demands and blood flow requirements of the body. (Figure 1.) Lately, the term 'heart failure' is preferred over the term 'congestive heart failure' (CHF) because not all patients display signs of being oedematous or overloaded with fluid.[1,2]

Based on the left ventricular ejection fraction (EF)—a parameter that has been widely used as a determining factor for patient selection during clinical trials—there are two main categories of HF, namely:[1]

- HF with preserved ejection fraction (HF*p*EF), and
- HF with reduced ejection fraction (HF*r*EF).

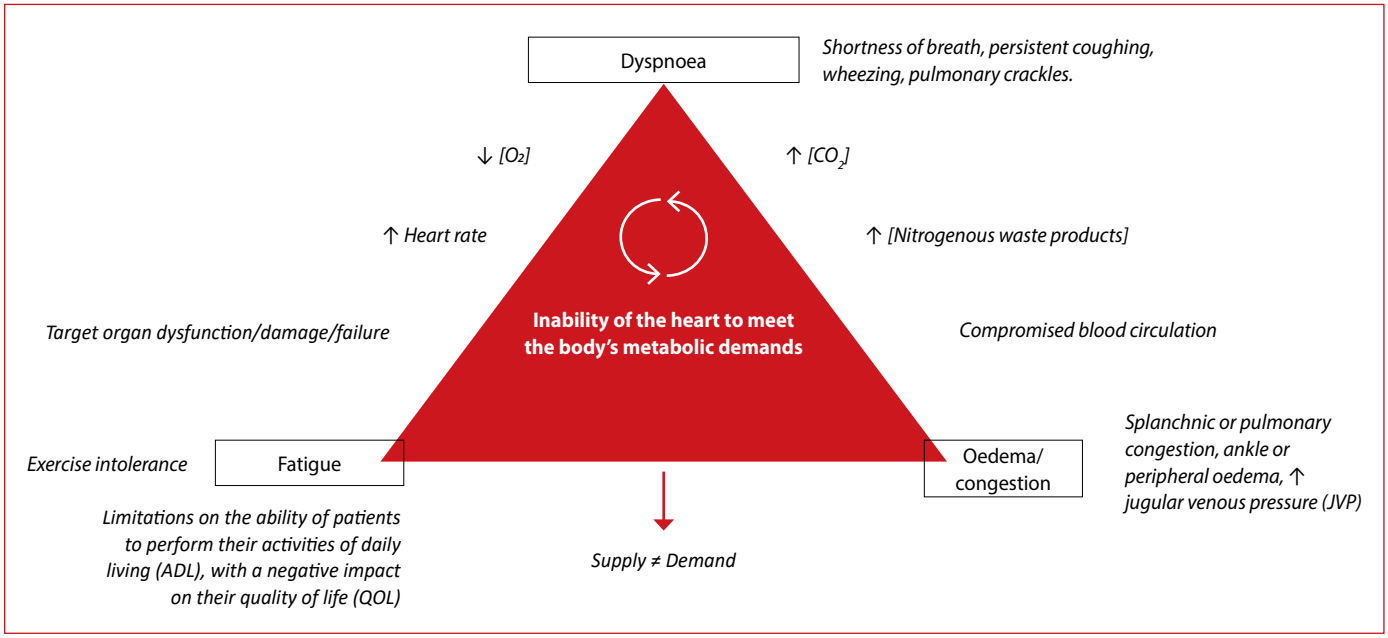

Figure 1: The heart failure 'triad' of dyspnoea, fatigue and oedema (patients do not always present with all three cardinal features in equal measure)[1,2]

The prognosis of HF remains poor, with more than 8% of adults admitted to hospital because of their deteriorating heart function, dying during their hospitalisation, and a third of those that have been discharged, may be expected to die within the ensuing 12 months. Thus, survival rates remain far from ideal.[3]

Brief epidemiology

The overall prevalence of adult HF in the global population is estimated to be around 1–2%. In the age group of 70 years and older, however, this number increases to around 10%, and roughly one-third of the adult population will have a lifetime risk of developing HF by the age of 55 years. The condition is also known to affect men in a slightly higher percentage than women. In terms of admissions and complications pertaining to hospital emergency units, HF accounts for around 5% of all such cases.[3]

In addition, the ageing global population and improvements in the management of HF itself, combined with better survival rates following acute myocardial infarction, are expected to result in further increases in the prevalence and disease burden of this condition.[4,5] In terms of the absolute mortality rate, approximately half of all patients with HF will die within five years of being diagnosed.[1]

The pathophysiology of heart failure

The most prominent and defining feature of HF, is the inability of the heart to meet the metabolic demands and blood flow requirements of the body. There are multiple causes and a variety of underlying conditions that may be implicated in the pathophysiological mismatch between metabolic supply and demand, and this often complicates the approach to treatment.[2,3]

Once the heart starts to fail, and a resultant inability to adequately supply in the blood flow and metabolic demands of the body ensues, a number of physiological, compensatory mechanisms are invariably activated. These so-called **neurohormonal compensatory mechanisms** initially limit the harmful effects of the failing heart on the systemic blood circulation, but eventually these mechanisms will result in a downward spiral of worsening cardiac output (CO) and upregulated neurohormonal responses.[3]

Normal cardiac output, and the interplay between stroke volume (SV) and the EF, are explained in Figure 2.

There are three major compensatory mechanisms that become activated when the CO decreases, as well as a number of additional mechanisms that augment these responses. The three major mechanisms are:

- **The sympathetic nervous system (SNS):** Noradrenaline, together with dopamine and adrenaline, are called the catecholamines. They constitute three different products, derived from three different stages of the same enzymatic conversion process, which utilises the amino acid, tyrosine, as its base substrate. Adrenaline, the neurohormone of the SNS, is released into the bloodstream by the secretory cells of the adrenal medulla. The latter should be viewed as an enlarged and specialised sympathetic ganglion. About 10% of the medullary cells produce and secrete noradrenaline. Roughly 80% to 90% of these cells contain the additional enzyme phenylethanolamine N-methyltransferase, which converts noradrenaline to adrenaline and therefore releases adrenaline into the bloodstream during stressful conditions such as anxiety, fear, pain, physical trauma and exertion, a sharp decrease in environmental temperature, or decreased cardiac output. In the context of cardiac failure, SNS stimulation increases the blood pressure via a potent pressor effect on peripheral arterioles, increases HR and the force of myocardial contraction via the cardiac β_1-adrenoceptors, and acts as one

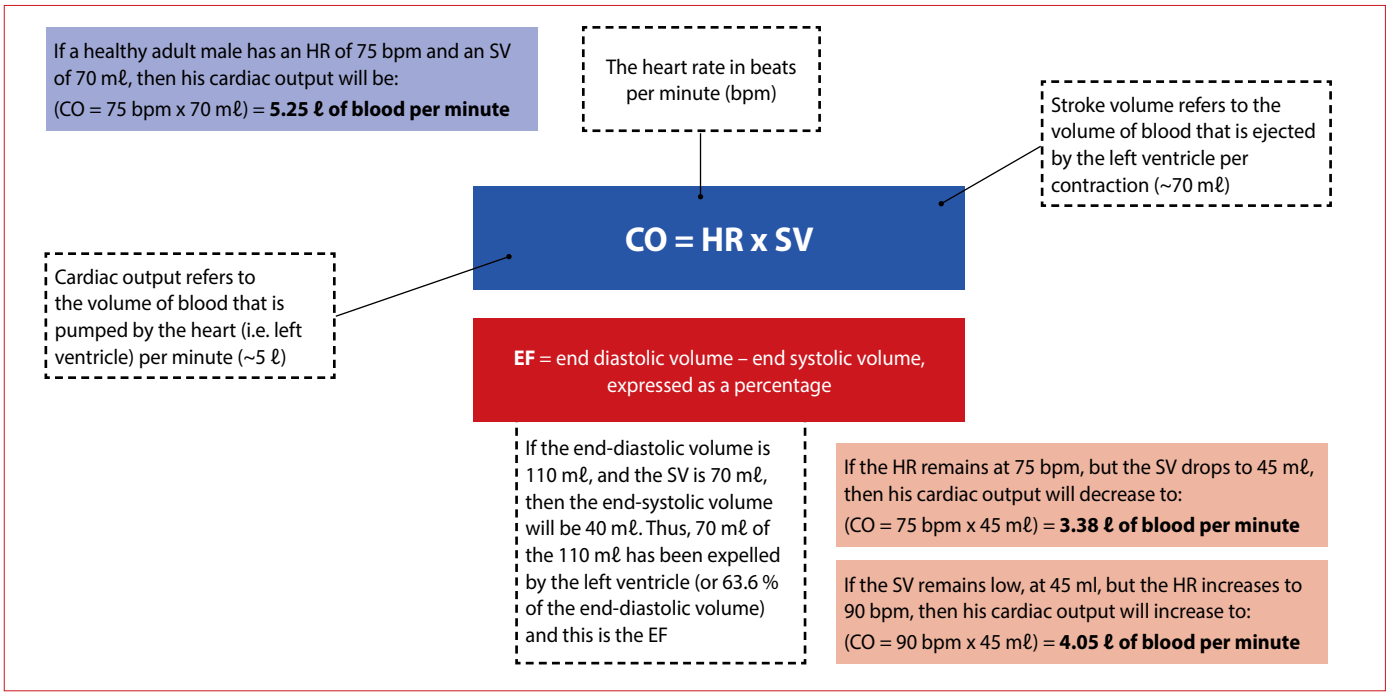

Figure 2: Cardiac output (CO) and the interplay between stroke volume (SV), heart rate (HR) and ejection fraction (EF)

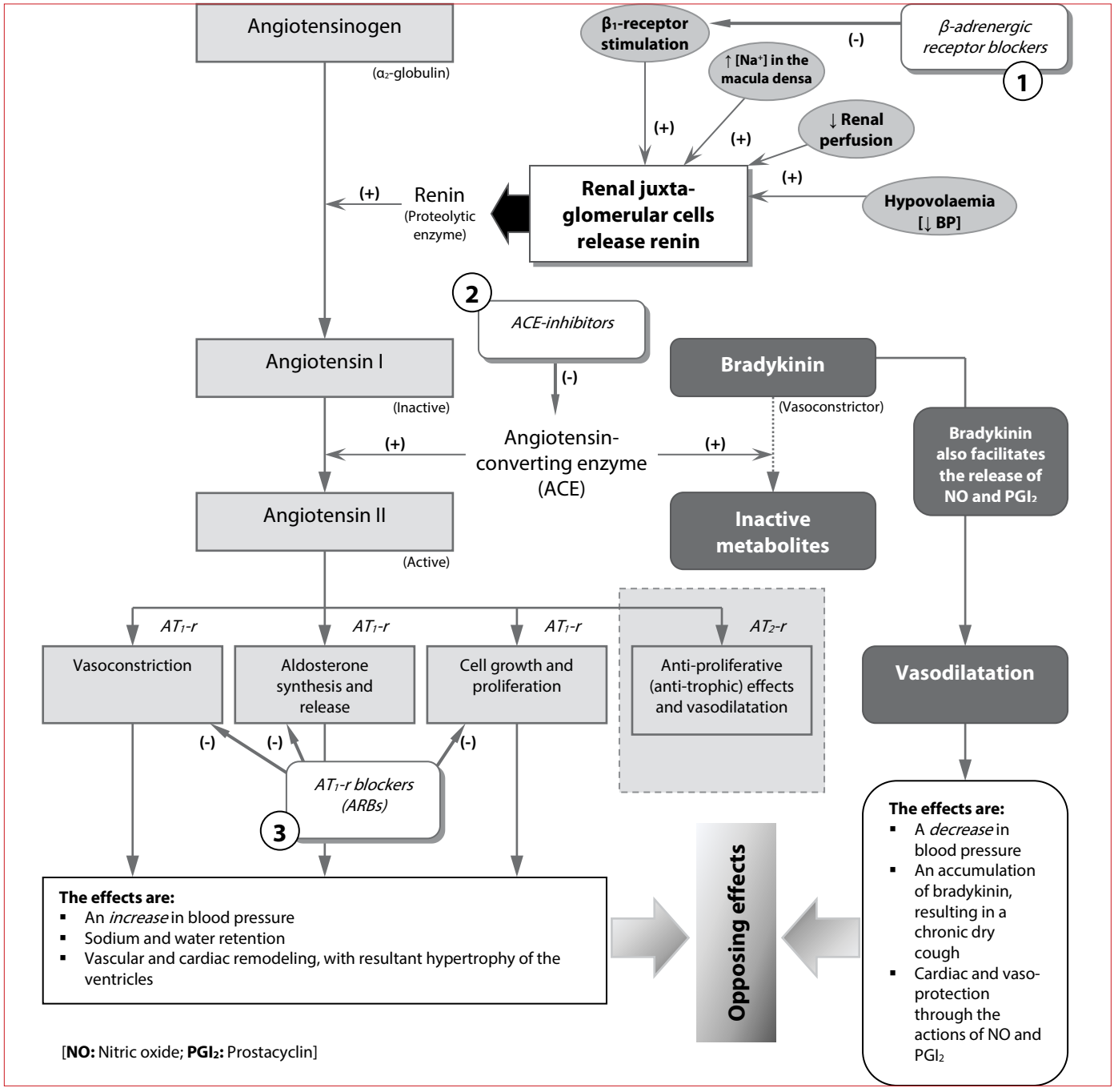

Figure 3: Diagram of the renin-angiotensin-aldosterone system (RAAS) showing the sites of action of (1) the β-adrenergic receptor blockers, (2) the ACE-inhibitors, and (3) the angiotensin II AT1-receptor blockers (ARBs)[2]

of the trigger mechanisms for the activation of the renin-angiotensin-aldosterone system (RAAS).[2]

- **The renin-angiotensin-aldosterone system (RAAS):** In patients with HF, it is the reduced renal perfusion that results in the activation of this intricate and potent compensatory mechanism. This results in a significant pressor effect, combined with sodium and water retention, and cardiac remodelling. Refer to Figure 3 for more details in this regard.[2,3]
- **The natriuretic peptide system (NPS):** The activation of the NPS actually serves to counteract the pressor effects of the SNS and the RAAS, as well as the accompanying sodium and water retention (via aldosterone release) and cardiac remodelling. The natriuretic peptides are released in response to an increase in ventricular (i.e. myocardial) wall tension.[3,6]

In the case of acute heart failure (AHF), which is the term used to refer to a new-onset or sudden worsening of existing signs and symptoms of HF, the characteristic clinical presentation is most often the result of significant congestion and fluid overload. The latter, in turn, is most likely the result of fluid redistribution within the body.

AHF frequently requires urgent intervention. Acute congestion may have dire consequences on the normal functioning of multiple organs and organ systems in the body, including the lungs, intestines, liver, kidneys and heart.[7]

Underlying risk factors

According to the American College of Cardiology Foundation/ American Heart Association (ACCF/AHA) Guideline for the Management of Heart Failure, the major risk factors that are associated with the development of HF are:[1]

- **Hypertension:** This is regarded as the *single most important modifiable risk factor* for the development of HF in the United States. Both systolic and diastolic hypertension require effective, long-term management to reduce the likelihood of the patient developing HF in the long run.
- **Diabetes mellitus:** Both obesity and insulin resistance are significant risk factors that will contribute to the development of HF.
- **Metabolic syndrome:** This syndrome requires any three of the following to be present in a given patient:
  - hypertension,
  - fasting hyperglycaemia,
  - low levels of HDL (high-density lipoprotein) cholesterol,
  - elevated triglyceride (TG) levels, or
  - abdominal obesity.

  Effective management of the high blood pressure levels, dyslipidaemia (typically regarded as elevated total cholesterol, elevated low-density lipoprotein [LDL] cholesterol, elevated TG levels, and low HDL cholesterol levels), diabetes mellitus, and excess body weight, will lower the chances of such a patient developing HF.
- **Atherosclerotic disease:** Patients that are known to suffer from existing atherosclerotic disease, are at a much higher risk of developing HF, whether the atherosclerosis affects the peripheral, cerebral and/or coronary blood vessels. Coronary artery disease (CAD) or acute coronary syndrome (ACS) are definite risk factors for the development of HF.

Other factors to consider, which may lead to or contribute towards the development of HF, include general obesity, tobacco use, and exposure to agents that are known to be cardiotoxic (such as certain chemotherapeutic agents). In addition, uncontrolled heart rate (HR), such as that seen in patients suffering from atrial fibrillation (AF), heavy alcohol use, the abuse of the recreational drugs cocaine and amphetamine, and in some patients, the presence of a genetic predisposition, are further examples of conditions that may lead to HF.[1]

Disease classification and severity

The classification of symptoms is often utilised in an attempt to grade the severity of a patient's condition. The most widely recognised functional classification system, is that of the New York Heart Association (NYHA) and is further illustrated in Figure 4.

In addition to the abovementioned NYHA functional classes, which are independent predictors of mortality,[1] there are a number of other classification systems for HF as well. Examples include the following:

- **The ACCF/AHA stages of HF:** According to this classification system, there are four stages, labelled A to D:[1]
  - **A:** The patient is at high risk, but without any structural heart disease or symptoms of HF.
  - **B:** Structural heart disease, but without signs or symptoms of HF.
  - **C:** Structural heart disease with prior or current symptoms of HF.
  - **D:** Refractory HF requiring specialised interventions.

  The treatment guidelines of the ACCF/AHA are based on these four stages. During stage A, the main aim is to modify the risk factors that are present, during stage B, to treat the structural heart disease, and during stages C and D, to try and reduce the associated morbidity and mortality.[1]
- **Left- and right-sided heart failure:** Irrespective of the ventricle, left or right, which was affected by the primary insult or

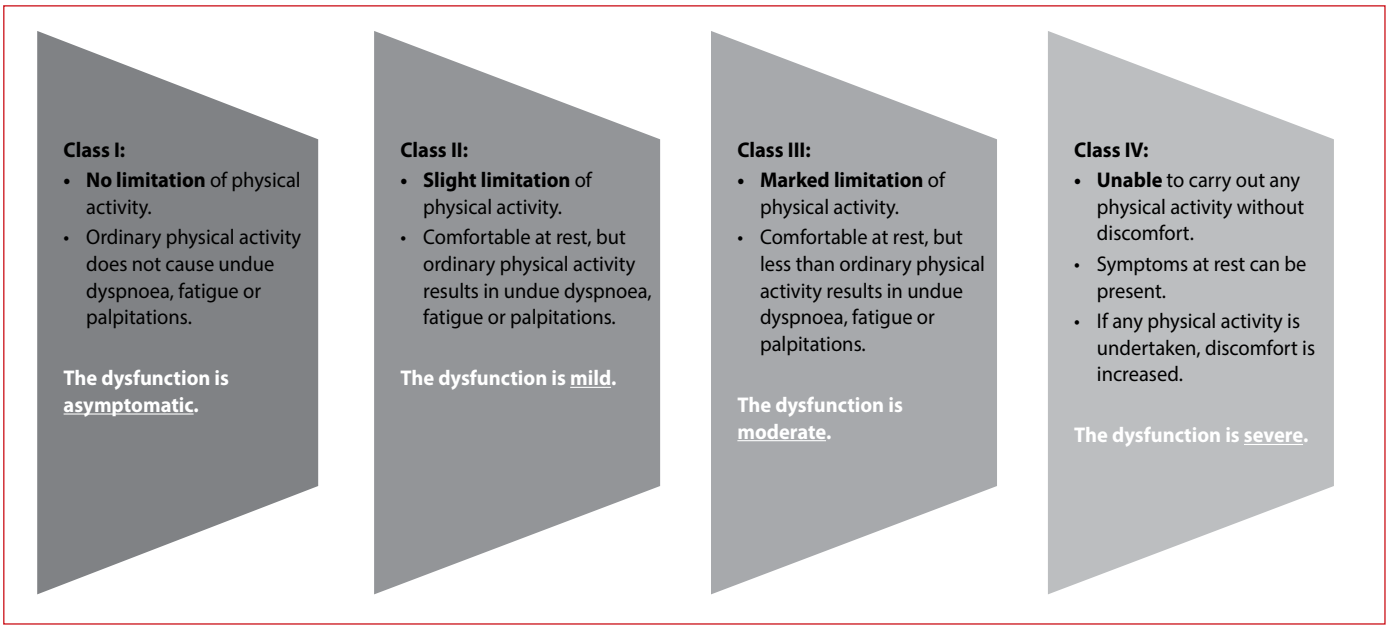

Figure 4: The stratified, functional classification of heart failure (Class I to IV) according to the New York Heart Association (NYHA)[1,3]

underlying pathology, it is often inevitable that both ventricles will ultimately fail. This is referred to as biventricular failure.[3]

- **Systolic versus diastolic dysfunction:** The former refers to the existence of a primary dysfunction in the contractility or pumping mechanism of the ventricle, as opposed to a problem that exists with the relaxation or subsequent filling of the cardiac chamber during diastole.[3] It is also common to find some elements of diastolic dysfunction in patients that have been diagnosed by primary systolic dysfunction.[1]
- **HF with preserved ejection fraction (HF*p*EF) versus reduced EF (HF*r*EF):** The ejection fraction may be measured non-invasively through the use of transthoracic echocardiography (ultrasound) and represents the percentage of blood being ejected by the left ventricle during a single cardiac contraction. The normal range is 55–70%. Patients with HF*p*EF usually have an EF of ≥ 50%; conversely, in HF*r*EF, the EF typically falls below the 40% mark (≤ 40%). Those patients that fall within the 41–49% range, constitute an intermediate or borderline group (HF*p*EF, *borderline*) and would be managed more like HF*r*EF patients than like those with a preserved EF. Lastly, there is a subset of HF*p*EF patients that would have previously had HF*r*EF and that now show an improvement or recovery in their EF to above the 40% level. These latter patients are classified as being HF*p*EF, *improved*.[1,3]

Recent advances in our understanding of the pathophysiology of HR have refocussed our attention on the diversity of causes that could result in this chronic condition, with the ensuing prospect of multiple subsets of patients, and which points to the fact that not all cases of HF can be or should be treated in the exact same way. HF*p*EF can no longer merely be viewed as a diastolic dysfunction of the heart, and HF*r*EF has progressed from a rapidly fatal disease into a chronic condition that requires long-term treatment strategies and support.[5]

Diagnosing heart failure

Given the fact that HF is a clinical syndrome, certain characteristic signs and symptoms (refer back to Figure 1) allow for a comprehensive medical history, combined with a thorough physical examination of the patient, to be used to arrive at a diagnosis of HF based on the clinical judgement of the clinician. This may be augmented by diagnostic tests that are mostly aimed at identifying the underlying cause and quantifying the severity of the condition. Non-invasive echocardiography should form part of the clinical assessment of the patient.[3]

The use of biomarkers in diagnosing heart failure

There are two specific natriuretic peptides that play an important part in the diagnosis and ongoing monitoring of patients with HF, namely:

- B-type natriuretic peptide (BNP), with the 'B' referring to the brain, and
- N-terminal pro-B-type natriuretic peptide (NT-proBNP).

Under normal circumstances, the heart continuously produces small amounts of $proBNP_{108}$, a 108-amino acid precursor peptide, which is subsequently cleaved to release the active hormone, called brain natriuretic peptide (BNP), and an inactive fragment, referred to as NT-proBNP. BNP is secreted from both the atria and the ventricles, as opposed to atrial natriuretic peptide, and is primarily produced in response to increased tension within the myocardial walls. Various factors may, however, result in such an increased wall tension, but especially including HF with a reduced left ventricular ejection fraction (LVEF). Elevated levels of BNP and NT-proBNP in this setting, are associated with poor outcomes. Clinicians should, however, also be aware of the fact that numerous other factors could potentially produce elevated levels of these biomarkers as well.[1,3,6]

A number of other, emerging biomarkers are currently being studied, or are awaiting validation, as well. Note that obesity may be associated with lower concentrations of the natriuretic peptides. In addition, it should also be noted that BNP (but not NT-proBNP, however) acts as a substrate for neprilysin, and this fact will have some significance in HF patients being treated with a neprilysin inhibitor (refer to the pharmacological treatment of heart failure).[8]

The role of the pharmacist in the pharmacological management of heart failure

Pharmacists may have multiple responsibilities in the care of HF, especially in a multidisciplinary team. This may differ from the different practice settings (inpatient vs outpatient) but a few services that may be rendered include medication reconciliation with associated patient medication education. This is important, especially in the geriatric population with polypharmacy. Equally important is providing pharmacotherapeutic recommendations and monitoring (including drug initiation, adjustment, and monitoring); early identification and prevention of adverse drug reactions and interactions; and improving medication adherence.

The two basic methodological approaches, from a pharmacological standpoint, to the management of HF, are to strengthen the force of myocardial contraction, and to decrease the cardiac workload. The latter, in turn, will decrease the myocardial oxygen demand. The increased workload is the result of failing myocardial contractility in the presence of compensatory sympathetic nervous system activity. This, in turn, results in tachycardia, improved myocardial contractility and increased peripheral resistance, and activation of the RAAS, which also causes vasoconstriction and an increased peripheral resistance, as well as sodium and water retention.[2]

Drugs that exert positive inotropic effects on the heart will strengthen the force of myocardial contraction to improve signs and symptoms of hypoperfusion, but this mechanism forces the myocardium to work harder and therefore increases its oxygen demand. Conversely, inhibition of the abovementioned neurohormonal pathways has the advantage of counteracting the detrimental effects of the compensatory vasoconstriction, increased peripheral resistance, and sodium and water retention seen in patients with chronic HF, without increasing myocardial oxygen demand. The positive inotropic agents are used in **acute settings** to maintain adequate vital organ perfusion.[2]

Drugs that strengthen the force of myocardial contraction

For myocardial contractility to increase (i.e. to produce a positive inotropic effect), the intracellular calcium-ion concentration needs to increase. In cardiac myocytes, cytosolic Ca^{2+} binds to troponin-C (one of the three subunits of troponin; the other two being troponin-I and troponin-T). The conformational change that follows then facilitates actin-myosin interaction, therefore allowing for the cardiac muscle to contract.[2]

DRUGS THAT CAUSE AN INCREASE IN INTRACELLULAR CALCIUM IONS[2]

- The cardiac or digitalis glycosides, such as digoxin, inhibit the Na^+-K^+-ATPase pump. This causes an accumulation of intracellular sodium ions. The sodium ions subsequently facilitate the intracellular movement of calcium ions through the sodium-calcium exchange mechanism.
- Digoxin also causes a heightened vagal nerve tone with subsequent negative chronotropic effects. It also has a direct negative dromotropic effect (i.e. it suppresses the SA-node, and also the conduction velocity through the AV-node). These effects oppose those of the sympathetic nervous system on the heart.
- Digoxin is also used in the management of atrial fibrillation (AF). It has a narrow therapeutic index and requires therapeutic drug monitoring.
- The β_1-receptor agonists, such as dobutamine, facilitate an increase in intracellular cAMP. This also causes the intracellular calcium ion concentration to be increased. Dobutamine and other suitable sympathomimetics are used in the management of acute cardiac failure where target organ perfusion is critically inadequate. Dopamine may also be used, especially in patients with low systolic blood pressure readings and cardiogenic shock. However, these drugs will also increase cardiac oxygen demand and myocardial workload.
- The phosphodiesterase (PDE) inhibitors, such as theophylline, also facilitate an increase in cAMP and subsequently of intracellular calcium ions. Theophylline is a non-selective PDE-inhibitor, as is caffeine. Milrinone (as well as amrinone) is an inhibitor of the PDE-3 isoform of phosphodiesterase. Furthermore, glucagon presents another way of achieving an increase in myocardial contractility through an increase in the synthesis of cAMP, and it is also especially useful in the treatment of a β-blocker overdose.

Drugs that decrease cardiac workload

Decreasing cardiac workload also decreases myocardial oxygen demand. Workload may be decreased through the dilatation of the veins, the arteries, or both. Venous dilatation will decrease central venous pressure, or CVP (i.e. cardiac preload), and dilatation of the arteries will decrease arterial blood pressure and peripheral resistance (i.e. cardiac afterload). However, facilitating selective arterial vasodilatation will elicit reflex tachycardia, due to the fact that the baroreceptors will interpret the drop in arterial blood pressure as hypovolaemia. This would be counterproductive when compared to the goals of the treatment plan.[2]

The most important aspect in the management of cardiac failure, however, is the **inhibition of the neurohormonal compensatory mechanisms** that give rise to the detrimental effects seen in patients with HF, such as fluid overload and oedema, hypoperfusion, and ventricular hypertrophy and cardiac remodelling. Cardio-selective β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and aldosterone antagonists may be employed to achieve an incremental neurohormonal inhibition. In addition, diuretics are used to manage the congestion and fluid overload.[2]

DRUGS THAT DECREASE THE CARDIAC PRELOAD[2]

- Diuretics: Hydrochlorothiazide is suitable for the treatment of chronic cardiac failure because its diuretic effects are not very potent. Furosemide is a powerful loop diuretic that lends itself to the management of AHF, while spironolactone and eplerenone antagonise aldosterone and its effects on the distal convoluted tubule of the nephron. Spironolactone and eplerenone are therefore regarded as potassium-sparing diuretics (and aldosterone antagonists).
- Venous dilators: Morphine, glyceryl trinitrate and other organic nitrates reduce the cardiac preload through direct venous dilatation.

DRUGS THAT DECREASE THE CARDIAC AFTERLOAD[2]

- Hydralazine is a direct-acting arteriolar vasodilator and elicits reflex tachycardia. This makes it unsuited for use in the treatment of cardiac failure, unless it is combined with a nitrate such as isosorbide dinitrate, or a β-blocker.
- Sodium nitroprusside is also direct-acting but dilates both arterioles and veins. Therefore, it does not elicit reflex tachycardia. It has the ability to spontaneously release nitric oxide (NO) from its molecular complex.

DRUGS THAT ANTAGONISE THE NEUROHORMONAL RESPONSE[2,8]

- Through inhibition of the angiotensin-converting enzyme (ACE), the so-called ACE-inhibitors, such as enalapril and perindopril, antagonise the RAAS. This effectively eliminates the vasopressor effects of angiotensin II, and also the sodium and water retention caused by aldosterone. The latter may also be directly antagonised by spironolactone and eplerenone.
- Furthermore, the ACE-inhibitors dilate both the arterial and the venous vascular beds. This effectively prevents a reflex tachycardia as well.
- Always be mindful of the fact that the ACE-inhibitors can cause angioedema, and that they need to be used with caution, and under close supervision, in patients with low systemic blood pressure readings, elevated serum potassium levels, and compromised kidney functioning.
- The angiotensin receptor blockers (ARBs) act as selective antagonists at AT_1-receptors. Examples include losartan, valsartan and candesartan. The ARBs are associated with much lower incidences of angioedema and the bradykinin-induced dry cough that is typically associated with the ACE-inhibitors, but the same cautions apply in terms of the systemic blood pressure, serum potassium levels and renal insufficiency.
- The selective β_1-adrenoceptor antagonists, such as bisoprolol and metoprolol, as well as carvedilol (the non-selective β-blocker and α_1-adrenoceptor antagonist) may be used to counteract the effects of the sympathetic nervous system in patients with cardiac failure.
- Ivabradine is a selective, so-called *funny* current (I_f) inhibitor that acts on the sinoatrial node and produces a selective and effective slowing of the HR, both at rest, and during physical exertion—refer to the separate subsection in the body text for more details.
- The newest addition to this group is the co-called ARNI, or angiotensin receptor neprilysin inhibitor, valsartan/sacubitril. This is a fixed-dose combination drug that combines the ARB, valsartan, with the neprilysin inhibitor, sacubitril. The latter inhibits the enzyme, neprilysin, which is responsible for the degradation of the natriuretic peptides, adrenomedullin, bradykinin and other vasoactive peptides. This product should also be used with caution in patients with low systemic blood pressure or renal insufficiency and may also cause angioedema.
- The ARNI should not be used concomitantly with an ACE-inhibitor, or within 36 hours of the last dosage of an ACE-inhibitor that the patient might have received. It is also contraindicated in patients with a history of angioedema.

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References: 1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics – 2015 Update. **2.** Emcor® South African approved PI. **3.** Cardicor® South African approved PI. S3 **Cardicor® 2,5 mg film-coated tablets.** Each tablet contains 2,5 mg bisoprolol. Reg. No.: 36/6.1/0457. S3 **Cardicor® 5 mg film-coated tablets.** Each tablet contains 5 mg bisoprolol. Reg. No.: 36/6.1/0458. S3 **Cardicor® 10 mg film-coated tablets.** Each tablet contains 10 mg bisoprolol fumarate. Reg. No.: 36/6.1/0459. S3 **Emcor® 2,5 mg film-coated tablets.** Each tablet contains 2,5 mg bisoprolol fumarate . Reg. No.: 51/6.1/1021. S3 **Emcor® 5 mg film-coated tablets.** Each tablet contains 5 mg bisoprolol fumarate. Reg. No.: 51/6.1/1022. S3 **Emcor® 10 mg film-coated tablets.** Each tablet contains 10 mg bisoprolol fumarate. Reg. No.: 51/6.1/1023. For full prescribing information (approved indications, contra-indications, warnings and special precaution) please refer to the package insert approved by the Medicines Regulatory Authority. **MERCK (Pty) Ltd.** Reg. No.1970/004059/07. 1 Friesland Drive, Longmeadow Business Estate South, Modderfontein, 1645.Tel. (011) 372-5000. Report adverse events to drug.safety.southeastafrica@merck-group.com or + 27 11 372 5304 (Fax line). June 2021. ZA-CAR-00016 March 2022.

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Treatment according to the ACCF/AHA stages A to D

The following is a brief synopsis of the main treatment recommendations per stage. (A detailed discussion does not fall within the scope of this article).

Stage A

Patients need to be optimally treated for their hypertension, dyslipidaemia, obesity and diabetes mellitus. Relevant and contemporary treatment guidelines need to be followed in this regard. In terms of hypertension, the following agents are known to be effective in helping to prevent HF in this setting: diuretic-based antihypertensive therapy, ACE-inhibitors, ARBs and suitable β-blockers. Patients need to be counselled in terms of other relevant risk factors, such as alcohol consumption, weight loss and the need to quit smoking. In the case of high blood pressure, both systolic and diastolic hypertension need to be controlled in the long term. The aldosterone antagonists are indicated in patients with refractory hypertension.[1]

Stage B

Generally speaking, all of the abovementioned recommendations for stage A HF should be applied to stage B as well. In patients with stage B HF with a reduction in LVEF, the ACE-inhibitors or, if needed, suitable β-blockers, are the agents of choice to improve morbidity and mortality in this setting. Should the ACE-inhibitors not be tolerated, the ARBs may be used as effective substitutes.[1]

Stage C

Patients with symptomatic HF require a sodium-restricted diet. In addition, those suffering from sleep apnoea may benefit from a suitable treatment intervention. Other measures that may warrant more serious consideration and that may have been deemed unnecessary in asymptomatic HF patients, include effective weight management, exercise training or regular physical activity, and the use of a cardiac rehabilitation programme, if indicated.[1]

Wherever appropriate, the pharmacological measures listed for stage A and B patients will also apply to stage C. To reduce morbidity and mortality in these patients, the following options may be utilised to achieve the goal of inhibiting the RAAS:[1,8]

- ACE-inhibitors, or ARBs, or an ARNI, in conjunction with
- an evidence-based β-blocker, and
- in selected patients, the addition of an aldosterone antagonist.

Selected and treatment-resistant patients should be evaluated for the need to add additional drugs to their treatment regimen, such as loop diuretics, digoxin, hydralazine, isosorbide dinitrate, anticoagulants, statins, a suitable second-generation calcium-channel blocker (i.e. amlodipine), etc. It is also recommended that symptomatic HF patients receive an omega-3 polyunsaturated fatty acid (PUFA) supplement, unless otherwise contraindicated.[1]

Another potential treatment option is the I_f channel inhibitor, ivabradine—see further down in the text, as well as the relevant text box, for more details.

Stage D

These are patients with advanced, refractory or end-stage cardiac failure, with a persistently increasing severity of their condition. The management of these severely ill patients does not fall within the scope of this article. Nevertheless, a few important measures or considerations that these patients will require are as follows:[1]

- Fluid restriction in the range of 1.5 to 2 litres per day.
- Inotropic support to preserve the functioning of their vital organs.
- The use of mechanical circulatory support, such as a ventricular assist device (VAD).
- In the case of very carefully selected and eligible patients, a heart transplantation is the ultimate treatment option for end-stage cardiac failure.

Ivabradine and heart failure

Ivabradine offers a different mechanism of action than many of the more traditional treatment approaches to HF. Ivabradine is a selective inhibitor of the I_f ion channel found in the cardiac pacemaker cells of the sinoatrial (SA) node. Ivabradine selectively blocks cardiac pacemaker cell I_f or *'funny'* current and exerts significant inhibition thereof at concentrations that do not affect other cardiac ionic currents.[9] Myocardial contractility and atrioventricular conduction are maintained while HR, both at rest and during exercise, is reduced.[10]

The I_f current is a mixed Na^+-K^+-inward ionic current, activated by hyperpolarisation, which determines the slope of the diastolic depolarisation, and in turn controls the rate at which the heart beats. It is one of the most important ionic currents for regulating pacemaker activity in the SA node.[11]

Ivabradine is an effective antianginal and anti-ischaemic drug, not inferior to the β-blocker, atenolol, and the calcium-channel antagonist (CCA), amlodipine.[12] It reduces the frequency of angina attacks and increases the time until the symptoms of angina start to appear during exercise or physical exertion. Ivabradine is not linked to the typical adverse reactions that are associated with the β-blockers or other antianginal drugs, because of its exclusive chronotropic effect (i.e. selectively lowering the HR).[12] In addition, it is indicated to reduce the risk of hospitalisation, for worsening HF, in patients with stable, symptomatic, chronic HF that are in sinus rhythm with an acceptable resting HR, and that are either on maximally tolerated dosages of β-blockers as well, or that have a contraindication to β-blocker use.[12,13]

Results from the SHI*f*T (Systolic Heart Failure Treatment with the *If* Inhibitor Ivabradine Trial) trial were published in 2010. SHI*f*T evaluated HR reduction through the direct sinus node inhibition of ivabradine. It was a multinational, randomised, placebo-controlled, parallel-group clinical trial in patients with moderate-to-severe HF and left-ventricular systolic dysfunction (with a 35% or lower LVEF, in sinus rhythm and with a HR of at least 70 beats per minute).[14] It was the first study conducted to

assess whether HR reduction by direct sinus node inhibition can decrease cardiovascular outcomes in patients with chronic HF and left ventricular systolic dysfunction.[10] It was found that ivabradine substantially reduced the major risks associated with HF when combined with guideline-based treatment.[14]

The importance of HR in the pathophysiology and clinical course of HF was confirmed by the SHI*f*T study. The beneficial effects of HR lowering with ivabradine have therefore been demonstrated by this study.[10,14]

Sacubitril and valsartan combination therapy

Sacubitril is the first in a new class of therapeutic agents to be made available on the local market. It is a neprilysin inhibitor and is currently available in combination with the ARB, valsartan. It is presently indicated as second-line treatment option for symptomatic HF, Class II, III or IV on the NYHA classification system, with systolic dysfunction.[1,8,13]

A previous neprilysin inhibitor, omapatrilat, also acted as an inhibitor of ACE and of aminopeptidase P, but its clinical development was halted due to concerns regarding the high incidence of angioedema associated with this drug. The ARNI is therefore contraindicated in patients with a history of angioedema.[8]

Non-pharmacological interventions

As mentioned in the previous section, a number of non-pharmacological measures form part of the treatment guidelines for HF. These include, but are not necessarily limited to:[1]

- Avoiding excessive alcohol consumption and the use of recreational drugs.
- Quitting the smoking habit (and/or other forms of tobacco use).
- Eating a healthy diet (with a firm sodium restriction where needed) and losing excess body weight.
- Sleep disorders are quite frequently observed in patients with HF, with more than 60% of adults with chronic HF having been found to suffer from either central or obstructive sleep apnoea. These patients may benefit significantly from the use of a device to provide continuous positive airway pressure (CPAP) during the night.
- Lastly, a number of invasive cardiac procedures, including coronary revascularisation, as well as mechanical devices, such as the implantable cardioverter-defibrillator (ICD) or the use of cardiac resynchronisation therapy (CRT), may be employed in the management of selected patients with cardiac failure.

Conclusion

HF patients have complex medication regimens that require the expertise of pharmacists as part of a multidisciplinary team. The interventions of the pharmacists may include medication reconciliation, educating patients and other healthcare professionals on their medications, which may collectively lead to a reduction in medication errors and drug interactions.

Further to this, the article provided a basic overview of the current trends and guidelines in the management of HF, including its classification, diagnosis, monitoring and treatment. According to the latest international guidelines, the most important differentiation in the setting of HF, is to determine which patients have HF*p*EF as opposed to HF*r*EF. The basis of HF treatment starts with the correct classification or grading of the severity of the patient's condition, the identification and management of modifiable risk factors, and then, the initiation of appropriate measures that are aimed at counteracting the detrimental effects of the neurohormonal response towards the mismatch in metabolic supply and demand, which is brought about by a failing heart.

References

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;62:e147-239. https://doi.org/10.1016/j.jacc.2013.05.019.
2. Schellack G. Pharmacology in clinical practice: Application made easy for nurses, pharmacists and allied health professionals. 3rd ed. Lansdowne: Juta and Company; 2016.
3. Wright P, Thomas M. Pathophysiology and management of heart failure. Clinical Pharmacist. 2018;10(12):online. Available from: https://www.pharmaceutical-journal.com/cpd-and-learning/cpd-article/pathophysiology-and-management-of-heart-failure/20205742.cpdarticle?firstPass=false#fn_3. Accessed 5 Mar 2020.
4. Metra M, Teerlink JR. Heart failure. Lancet. 2017;390(10106):1981-95. https://doi.org/10.1016/S0140-6736(17)31071-1.
5. Udelson JE, Stevenson LW. The future of heart failure diagnosis, therapy, and management. Circulation. 2016;133(25):2671-86. https://doi.org/10.1161/CIRCULATIONAHA.116.023518.
6. Bay M, Kirk V, Parner J, et al. NT-proBNP: A new diagnostic screening tool to differentiate between patients with normal and reduced left ventricular systolic function. Heart. 2003;89(2):150-54. https://doi.org/10.1136/heart.89.2.150.
7. Arrigo M, Parissis JT, Akiyama E, Mebazaa A. Understanding acute heart failure: Pathophysiology and diagnosis. Eur Heart J. 2016;18(Suppl G):G11-G18. https://doi.org/10.1093/eurheartj/suw044.
8. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol. 2017;70:776-803. https://doi.org/10.1016/j.jacc.2017.04.025.
9. DiFrancesco D, Camm JA. Heart rate lowering by specific and selective If current inhibition with ivabradine: A new therapeutic perspective in cardiovascular disease. Drugs. 2004;64(16):1757-65. https://doi.org/10.2165/00003495-200464160-00003.
10. Cowie MR. Ivabradine: The start of a SHIFT in heart failure treatment. Interv Cardiol. 2013;5(1):415-26.
11. Tardif JC, Ford I, Tendera M, Bourassa MG, Fox K. Efficacy of ivabradine, a new selective If inhibitor, compared with atenolol in patients with chronic stable angina. Eur Heart J. 2005;26(23):2529-36. https://doi.org/10.1093/eurheartj/ehi586.
12. Marquis-Gravel G, Tardif JC. Ivabradine: The evidence of its therapeutic impact in angina. Core Evid. 2008;3(1):1-12.
13. Snyman JR, editor. Monthly Index of Medical Specialities. 2020;59(11).
14. Swedberg K, Komajda M, Böhm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): A randomised placebo-controlled study. Lancet. 2010;376(9744):875-85. https://doi.org/10.1016/S0140-6736(10)61198-1.

The pharmacological management of hypothyroidism

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Abstract

Hypothyroidism is a condition characterised by the biochemical and clinical manifestations of deficient thyroid hormone concentrations.[1] Worldwide, the most common cause of this condition is iodine deficiency. In cases where iodine deficiency is not the cause, the most common causes of hypothyroidism are Hashimoto's thyroiditis, thyroidectomy and radioactive iodine treatment.[2] Apart from thyroid gland pathology (primary hypothyroidism), hypopituitarism (secondary hypothyroidism) should also be considered.[2] Autoimmune hypothyroidism occurs at a mean annual rate of 4 per 1 000 women and 1 per 1 000 men.[2] The onset of hypothyroidism is usually insidious, and patients may only become aware of symptoms after optimal thyroid hormone replacement. Typical signs include a puffy face, oedematous eyelids, non-pitting pretibial oedema, dry, brittle hair, alopecia, thinning of the outer third of the eyebrows, pallor and retarded nail growth.[2] Goiter is sometimes the presenting symptom in Hashimoto's thyroiditis, but typical symptoms like fatigue, dry skin, hair loss, constipation, cold intolerance and weight gain may also be present. The aim of therapy is to improve symptoms, normalise serum thyroid-stimulating hormone (TSH), reduce the goiter size and to avoid overtreatment.[3,4]

Keywords: hypothyroidism, pharmacological management, deficient thyroid hormone concentrations

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Spectrum and diagnosis of hypothyroidism

Subclinical hypothyroidism

The prevalence of subclinical hypothyroidism varies from 4–20% within the adult population. This condition is identified by an abnormal thyroid function test in the absence of obvious symptoms.[5] An elevated TSH with normal triiodothyronine (T_3) and thyroxine (T_4) levels is the hallmark of subclinical hypothyroidism.[5] Although it may be associated with cardiovascular disease and a substantial number of patients progress to primary hypothyroidism, treatment is not always indicated.[3,6]

Primary hypothyroidism

In this condition, the thyroid gland is unable to produce sufficient thyroid hormone to meet the body's requirements.[6] The diagnosis is based on an elevated TSH level associated with T_3 and T_4 levels below the normal reference range.[6] Unless the primary hypothyroidism is reversible or transient, all patients with this condition must receive replacement therapy.[3]

Central (secondary) hypothyroidism

This condition is due to pathology of the pituitary gland or hypothalamus causing impaired release of TSH and/or thyrotropin-releasing hormone.[2,6] A low T_4 in the setting of a low or inappropriate TSH level is suggestive of central hypothyroidism.[2] Potential causes are surgery, trauma, tumours and infiltrative disorders of the pituitary gland or hypothalamus.[2]

Who must be treated?

All cases of primary and central hypothyroidism require treatment, except if the hypothyroidism is transient.[3] Conversely, based on TSH levels, the approaches listed in Table I are recommended for managing subclinical hypothyroidism.

Table I: Treatment for subclinical hypothyroidism

TSH	Who should be treated?
TSH ≥ 10 mIU/L	All patients should be treated[3,7]
TSH 7–9.9 mIU/L	Patients younger than 65–70 years due to the increased risk of cardiovascular mortality in this group[3,7,8] Patients older than 65–70 years with hypothyroidism symptoms[3,7]
TSH of above upper limit of normal to 6.9 mIU/L	Patients younger than 65–70 years with convincing symptoms[3] In older patients the upper limit of the TSH is physiologically elevated and therefore does not warrant treatment in this range[7,9]

Pharmacology of available treatment options

Levothyroxine

Levothyroxine is a synthetic levorotatory isomer of thyroxine and has been the gold standard for treatment since the 1960s.[10] In South Africa, levothyroxine sodium is available as tablets for oral administration. Approximately 80% of this compound is absorbed in the stomach and small intestine and absorption can be improved by taking it on an empty stomach.[10,11] The tablet is taken daily and has a long $t_{1/2}$ of seven days. Owing to this long $t_{1/2}$ it does not have much of an effect on TSH and T_4 levels when a dose is skipped.[11]

Table II: Factors affecting levothyroxine treatment

Mechanism	Example
Impaired absorption	• Proton pump inhibitors and aluminium containing antacids • Bile acid sequestrants • Calcium carbonate and iron salts • Lactose intolerance • *H. pylori* infection • Atrophic gastritis • Celiac disease • Foods like soy bean, papaya and grapefruit[12]
Increased metabolism	• Rifampicin • Carbamazepine • Phenytoin • Sertraline
Impairment of the peripheral conversion of T_4 to T_3	• Amiodarone
Uncertain mechanism	• Oestrogen • Pregnancy • Some of the statins and tyrosine kinase inhibitors used to treat certain malignancies
Decreased dosage requirements	• Older than 65 years • Androgen therapy in women
Decrease in TSH without an effect on T_3 and T_4	• Metformin

Table II describes several factors that may influence therapy with levothyroxine.[10,11]

Autoimmune gastritis is a potential cause that needs to be considered when thyroxine replacement doses exceed the theoretical requirements in patients treated for autoimmune thyroiditis.[13]

In South Africa, levothyroxine is available as tablets of different strengths. Some of these are also scored, and dose titration increments of 12.5 mcg are possible. Soft gel and liquid formulations are designed to improve bioavailability, but in a recent trial, the evidence for using these formulations was weak, and further studies are needed.[14]

Liothyronine

Daily production of T_3 by the thyroid gland is inadequate for the demands of the body. Approximately 80% of the produced T_4 is disposed of by the peripheral conversion of T_4 to T_3 by deiodination.[12,15,16] Of both the active thyroid hormones, T_3 is the more active due to a 10-fold greater affinity of the cell nucleus for T_3.[12,15]

Liothyronine sodium is a salt of T_3 and is available as a tablet in South Africa. In contrast to levothyroxine, this salt is absorbed almost completely after oral ingestion. The shorter $t_{1/2}$ of 18–24 h of this compound makes it necessary to administer liothyronine sodium more than once a day and treatment with this compound may cause transient elevations of the serum T_3 above the normal range.[6,11]

Treatment of hypothyroidism

Levothyroxine monotherapy

Monotherapy with levothyroxine is the preferred form of treatment for hypothyroidism and is recommended in various published meta-analyses as well as national and international guidelines.[2-4,17-21]

Levothyroxine/Liothyronine combination therapy

Combination therapy is a controversial topic. Although the majority of studies are in favour of levothyroxine monotherapy,[4,18] a subpopulation of approximately 10–15% of optimally treated patients with residual symptoms of hypothyroidism is recognised.[1,22-25] The various explanations for these residual symptoms are as follows:

- The basal metabolic rate in patients treated with levothyroxine is approximately 10% slower than that of normal controls despite TSH levels in the normal range. This might be the result of lower free T_3 levels causing relative tissue hypothyroidism.[26,27]
- The peripheral conversion capacity of T_4 to T_3 is a heterogenous process, with 20% of patients on levothyroxine that do not achieve adequate free T_3 concentrations while they are in the normal reference range for TSH.[21,28]
- In rats, it has been shown that the T_4 to T_3 conversion process is inhibited by T_4. The inhibition is more pronounced in the peripheral tissues and less pronounced in the hypothalamus. The preservation of T_3 production in the hypothalamus may be responsible for normal suppression of TSH in contrast to the low T_3 and increased T_4:T_3 ratio in the peripheral tissues.[29]
- Failure of randomised controlled trials to prove superiority of levothyroxine/liothyronine combination therapy may be a result of the inadequate design of these trials.[30]

Residual hypothyroidism symptoms should not immediately be attributed to inadequate thyroid hormone treatment and other potential causes (such as endocrine disorders, autoimmune disorders, haematological conditions, end-organ damage, nutritional deficiencies, metabolic syndromes, concomitant drugs or lifestyle) for these symptoms should be excluded.[21,25,31]

Suggested candidates for treatment with combined levothyroxine/liothyronine therapy are (i) patients with persistent hypothyroidism symptoms after thyroidectomy or ablative therapy with radioiodine[3,21,31] despite optimal levothyroxine therapy and (ii) patients on optimal levothyroxine treatment that experience persisting symptoms and who have a serum T_3 level at or below the lower limit of the T_3 reference range.[3]

Levothyroxine/liothyronine combination therapy is not recommended either in pregnant women or in patients with cardiac dysrhythmias, and should be stopped if patients do not experience an improvement in their symptoms after three months of treatment.[1,21,31]

Initiation of therapy

Levothyroxine monotherapy

The levothyroxine monotherapy replacement dose varies in patients with different aetiologies of hypothyroidism and is dependent on the residual functionality of the thyroid tissue.[32] In post thyroidectomy patients without any residual thyroid tissue functionality, a full replacement dose can be calculated based on BMI rather than weight-based dosing, due to a tendency to overdose overweight and underdose normal weight patients.[33] The mean euthyroid dose stratified according to BMI is given in Table III.[33]

Table III: Mean euthyroid dose stratified according to BMI

BMI	Mean euthyroid dose in mcg/kg/day
≤ 24.99	1.84
25.00–29.99	1.63
30.00–34.99	1.50
≥ 35.00	1.39

The average full replacement dose is 1.6 mcg/kg/day and may be prescribed for patients under the age of 65 years without a history of ischaemic heart disease. On this dose, it takes about four weeks for the free T_4 (FT_4) concentration to normalise.[3,34]

Where there is still residual thyroid function, in older patients or if there is a history of ischaemic heart disease, a lower dose of 25–50 mcg per day should be initiated and adjusted over time.[3] Although the FT_4 normalises faster when the full replacement dose is given, there is no difference in the time it takes for symptoms and quality of life to improve when a full replacement approach is compared to a low starting dose adjusted over time.[3,34]

Levothyroxine/liothyronine combination therapy

The ultimate goal of combination therapy is to improve the residual hypothyroidism symptoms in patients with a normal TSH.[1] Liothyronine is three to four times more potent than levothyroxine which means that 12.5 mcg liothyronine plus 50 mcg levothyroxine is equal to 100 mcg thyroxine.[3,31] The secretion ratio of T_4:T_3, with an average of 16:1 (13:1–20:1), and the potency of liothyronine must be taken into account when the dose of the different components of the combination therapy is calculated.[1] The calculation of the components are as follows:[1,3]

- To calculate T_3: Daily dose of T_4 that normalises TSH divided by 17 (to approach the physiological T_4:T_3 ratio of 16:1).
- To calculate T_4: Subtract 3xT_3 from T_4 (daily dose).
- In South Africa, it is almost impossible to prescribe the physiologically correct dose of liothyronine since the only liothyronine preparation currently available is Tertroxin 20 mcg tablets. These tablets are scored so that a minimum dose of 10 mcg can be given, which is still too much in most patients.

One can also use Table IV to convert levothyroxine monotherapy to levothyroxine/liothyronine combination therapy.[1,3]

Table IV: Convert levothyroxine monotherapy to levothyroxine/liothyronine combination therapy

	Combination therapy	
Current T_4 therapy	T_4 dose	T_3 dose
75–100 mcg	50–75 mcg	2.5 mcg bd
112–137mcg	88–112 mcg	2.5 mcg tds or 5 mcg mane and 2.5 cg nocte
150–175 mcg	112–137 mcg	5 mcg bd
200–250 mcg	150–200 mcg	7.5 mcg mane and 5 mcg nocte

Appropriate administration of thyroid replacement medication

Absorption of levothyroxine is affected by many factors, as mentioned earlier, and it has been shown that non-fasting regimens are associated with an increase in both the level and variability of TSH.[35] An interesting study that evaluated the optimal timing of administration of levothyroxine found that there was no difference in the absorption between morning, noon and bedtime administration of levothyroxine.[36] From the above, we can deduct that taking levothyroxine in the fasting state is more important than the time of day that it is taken. To prevent impaired absorption due to food, the levothyroxine must be taken 60 minutes before breakfast in the fasting state and at least 3 hours after supper when taken at bedtime.[4]

No specific administration regimen has been suggested for liothyronine.

Monitoring and adjustment of therapy

Levothyroxine monotherapy

After initiation of levothyroxine therapy, patients can expect an improvement in their symptoms within two weeks. However, in severe cases, recovery can take months. The TSH level is used as a parameter to adjust levothyroxine therapy.[3,4,19] It is recommended that the TSH is collected before the morning levothyroxine is taken.[1] The TSH level must be measured every six weeks and the levothyroxine adjusted accordingly.[3,4] Depending on the TSH value, the levothyroxine is adjusted in increments of 12.5–25 mcg. Downward adjustment is necessary for a low TSH and an increase in dose is required for an elevated TSH level.[3,4,19] After optimal replacement with levothyroxine is achieved, the TSH level should be measured every 6–12 months.[4,19]

The goal in secondary hypothyroidism is to maintain the FT_4 in the upper half of the reference range. However, in older patients or patients with comorbidities at risk of treatment complications, a lower FT_4 value can be accepted.[4] The FT_4 should, like the TSH, be measured every 4–8 weeks until an optimal dose of levothyroxine is reached. Thereafter, the FT_4 should be measured every 6–12 months to monitor therapy.[19]

Levothyroxine/liothyronine combination therapy

Monitoring of combination therapy should be done by measuring TSH, FT_4 and free T_3 (FT_3), and calculating the FT_4/FT_3 ratio on serum collected before the morning dose.[1,20]

The aim is to achieve normal values for all the markers. If adjustment of therapy is necessary, it is suggested that only one of the components be adjusted, preferably liothyronine.[1,20] An alternative approach is to measure only the TSH and FT_4 since FT_3 values fluctuate too much during the day and is actually a reflection of the interval since the last dose of liothyronine.[3] The markers should be repeated every six weeks until the patient is euthyroid, after which it must be followed up every 6–12 months.[3]

Special patient groups

The elderly

TSH levels, as well as thyroid antibodies, increase as people age. Owing to the increase in the TSH concentration, elderly patients can still be euthyroid with a TSH value above the upper limit of normal. The presence of anti-thyroid antibodies does not predict development of thyroid disease in the elderly.[4,19]

Older people (> 65 years) are more susceptible to the adverse effects of thyroid hormone overreplacement, and treatment with levothyroxine should be initiated with low dosages and gradually titrated upwards, bearing in mind that a slightly elevated TSH might be appropriate.[4,29,37]

Coronary heart disease

Although thyroid hormone replacement therapy has a positive inotropic and chronotropic level on the myocardium and can lead to angina in patients with severe ischaemic heart disease, symptoms may actually improve or, in asymptomatic patients, initially not appear when treatment is initiated.[3,4] Owing to the risk of angina in this patient group, it is recommended that patients should be started on low doses of levothyroxine followed by a gradual increase in dose. The use of β-adrenergic blocking drugs make optimal treatment possible in most patients.[4,38]

Pregnancy

The fetal thyroid gland only starts contributing to the thyroid hormone requirements of the fetus during the second half of gestation and the fetus is therefore dependent on the mother's thyroid hormones for normal neurological development.[39] Hypothyroidism in pregnant women, even when mild and still asymptomatic, can adversely affect their children's neuropsychological development.[40] Elevated TSH levels during pregnancy can also lead to the following adverse obstetric outcomes:

- Increased caesarean section rate in both overt and subclinical hypothyroidism.[41]
- Increased rate of fetal death.[42]
- Increased rate of spontaneous pregnancy loss.[43]
- Increased risk of placental abruption and preterm delivery.[44]

Subclinical and overt hypothyroidism should be managed on an urgent basis and replacement therapy in overt hypothyroidism should be managed by initiating full replacement therapy.[45]

The following is a general guide to levothyroxine dosing:[46]

- TSH: > 4 mIU/L with a low T_4: approximately 1.6 mcg/kg/day
- TSH: > 4 mIU/L with a normal T_4: approximately 1.0 mcg/kg/day
- TSH: 2.6–4 mIU/L low dose initiation

Levothyroxine requirements during pregnancy increases by approximately 30–50%.[47,48]

Goals of levothyroxine replacement during pregnancy are:[45,46]

- TSH less than 2.5 mIU/L prior to conception; however, some experts prefer a preconception TSH of < 1.2 mIU/L.
- TSH of less than 2.5 mIU/L or in the lower half of the trimester-specific reference range during the pregnancy.

The TSH should be measured every 4–6 weeks and the levothyroxine adjusted accordingly.[38]

Oestrogen therapy

Oestrogen therapy may increase the need for levothyroxine in thyroid hormone replacement patients and the TSH concentration should be measured 6–12 weeks after initiation of oestrogen therapy. Dosage adjustments may also be required in young women on thyroid replacement therapy when an oral contraceptive is prescribed.[3]

Surgical patients

Post-surgical patients that are unable to eat for a few days should receive replacement therapy via the parenteral route.[3]

Conclusion

The spectrum of hypothyroidism consists of subclinical hypothyroidism, primary hypothyroidism and secondary hypothyroidism. It is important to diagnose and adequately treat this biochemical abnormality since it is associated with an increased risk for the development of ischaemic heart disease and other conditions. Subclinical hypothyroidism does not always need to be treated, but primary and secondary hypothyroidism should be managed with thyroid hormone replacement therapy. Levothyroxine is the mainstay of treatment but combination therapy with levothyroxine/liothyronine is indicated in a small percentage of patients. Combination therapy is still controversial and should be reserved for patients where other causes of persistent hypothyroidism symptoms have been excluded. Combination therapy should be stopped if symptoms are still present after three months of optimal therapy. The dose of the initiation of therapy will depend on the residual amount of functioning thyroid tissue. A full replacement dose is given after surgical removal of the thyroid gland but patients with residual thyroid function are started on lower dosages and titrated upwards until euthyroid. In elderly patients and patients with ischaemic heart disease, low-dose replacement therapy is initiated due to the risk of adverse effects of overreplacement of thyroid hormones. Pregnant women and women planning on falling pregnant should be carefully monitored and optimally supplemented to avoid the fetal and obstetric complications associated with hypothyroidism.

References

1. Wiersinga WM, Duntas L, Fadeyev V, Nygaard B, Vanderpump MPJ. 2012 ETA guidelines: the use of L-T4 + L-T3 in the treatment of hypothyroidism. Eur Thyroid J. 2012;1(2):55-71. https://doi.org/10.1159/000339444.
2. Jameson JL, Mandel SJ, Weetman AP. Hypothyroidism. In: Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Los, editors. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill; 2018. p. 2698-702.
3. Ross DS. Treatment of primary hypothyroidism in adults [Internet]. In: Cooper DS, Mulder JE, editors. UpToDate. 2019. Available from: https://www.uptodate.com/contents/treatment-of-primary-hypothyroidism-inadults?search=hypothyroidismtreatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed 17 Jan 2021.
4. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. Thyroid. 2014;24(12):1670-751. https://doi.org/10.1089/thy.2014.0028.
5. Cooper DS, Biondi B. Subclinical thyroid disease. Lancet. 2012;379(9821):1142-54. https://doi.org/10.1016/s0140-6736(11)60276-6.
6. McDermott MT. Hypothyroidism. Ann Intern Med. 2020;173(1):ITC1-16. https://doi.org/10.7326/aitc202007070.
7. Biondi B, Cappola AR, Cooper DS. Subclinical hypothyroidism: a review. JAMA. 2019;322(2):153-60. https://doi.org/10.1001/jama.2019.9052.
8. Rodondi N, Den Elzen WPJ, Bauer DC, et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA. 2010;304(12):1365-74. https://doi.org/10.1001/jama.2010.1361.
9. Mooijaart SP, Du Puy RS, Stott DJ, et al. Association between levothyroxine treatment and thyroid-related symptoms among adults aged 80 years and older with subclinical hypothyroidism. JAMA. 2019;322(20):1977-86. https://doi.org/10.1001/jama.2019.17274.
10. Skelin M, Lucijanić T, Amidžić Klarić D, et al. Factors affecting gastrointestinal absorption of levothyroxine: a review. Clin Ther. 2017;39(2):378-403. https://doi.org/10.1016/j.clinthera.2017.01.005.
11. Brent GA, Koenig RJ. Thyroid and antithyroid drugs. In: Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman and Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill; 2018. p. 787-802.
12. Colucci P, Yue CS, Ducharme M, Benvenga S. A review of the pharmacokinetics of levothyroxine for the treatment of hypothyroidism. Eur Endocrinol. 2013;9(1):40-7. https://doi.org/10.17925/EE.2013.09.01.40.
13. Checchi S, Montanaro A, Pasqui L, et al. L-thyroxine requirement in patients with autoimmune hypothyroidism and parietal cell antibodies. J Clin Endocrinol Metab. 2008;93(2):465-9. https://doi.org/10.1210/jc.2007-1544.
14. Nagy EV, Perros P, Papini E, Katko M, Hegedus L. New formulations of levothyroxine in the treatment of hypothyroidism: trick or Treat? Thyroid. 2020;31(2):193-201. https://doi.org/10.1089/thy.2020.0515.
15. Mandel SJ, Brent GA, Larsen PR. Levothyroxine therapy in patients with thyroid disease. Ann Intern Med. 1993;119(6):492-502. https://doi.org/10.7326/0003-4819-119-6-199309150-00009.
16. Lopresti JS, Eigen A, Kaptein E, et al. Alterations in 3,3',5'-triiodothyronine metabolism in response to propylthiouracil, dexamethasone, and thyroxine administration in man. Metab Clin Exp. 1989;84(November):1650-6.
17. De Carvalho GA, Paz-Filho G, Junior CM, Graf H. Pitfalls on the replacement therapy for primary and central hypothyroidism in adults. Eur J Endocrinol. 2018;178(6):R231-44. https://doi.org/10.1530/EJE-17-0947.
18. Grozinsky-Glasberg S, Fraser A, Nahshoni E, Weizman A, Leibovici L. Thyroxinetriiodothyronine combination therapy versus thyroxine monotherapy for clinical hypothyroidism: meta-analysis of randomized controlled trials. J Clin Endocrinol Metab. 2006;91(7):2592-9. https://doi.org/10.1210/jc.2006-0448.
19. Dave JA, Klisiewicz A, Bayat Z, et al. SEMDSA/ACE-SA guideline for the management of hypothyroidism in adults [Internet]. SA Pharm J. 2016;83(2):34-43. Available from: http://www.jemdsa.co.za/index.php/JEMDSA/article/view/497. Accessed 17 Jan 2021.
20. Okosieme O, Gilbert J, Abraham P, et al. Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee. Clin Endocrinol. 2016;84(6):799-808.
21. Wiersinga WM. Paradigm shifts in thyroid hormone replacement therapies for hypothyroidism. Nat Rev Endocrinol. 2014;10(3):164-74. https://doi.org/10.1038/nrendo.2013.258.
22. McAninch EA, Bianco AC. The history and future of treatment of hypothyroidism. Ann Intern Med. 2016;164(1):50-6. https://doi.org/10.7326/M15-1799.
23. Saravanan P, Chau WF, Roberts N, et al. Psychological well-being in patients on "adequate" doses of L-thyroxine: results of a large, controlled community-based questionnaire study. Clin Endocrinol. 2002;57(5):577-85. https://doi.org/10.1046/j.1365-2265.2002.01654.x.
24. Peterson SJ, Cappola AR, Castro MR, et al. An online survey of hypothyroid patients demonstrates prominent dissatisfaction. Thyroid. 2018;28(6):707-21. https://doi.org/10.1089/thy.2017.0681.
25. Hennessey JV, Espaillat R. Current evidence for the treatment of hypothyroidism with levothyroxine/levotriiodothyronine combination therapy versus levothyroxine monotherapy. Int J Clin Pract. 2018;72(2):1-14. https://doi.org/10.1111/ijcp.13062.
26. Gorman CA, Jiang N-S, Ellefson RD, Elveback LR. Comparative effectiveness of dextrothyroxine and levothyroxine in correcting hypothyroidism and lowering blood lipid levels in hypothyroid patients. J Clin Endocrinol Metab. 1979;49(1):1-7. https://doi.org/10.1210/jcem-49-1-1.
27. Samuels MH, Kolobova I, Smeraglio A, et al. Effects of levothyroxine replacement or suppressive therapy on energy expenditure and body composition. Thyroid. 2016;26(3):347-55. https://doi.org/10.1089/thy.2015.0345.
28. Gullo D, Latina A, Frasca F, et al. Levothyroxine monotherapy cannot guarantee euthyroidism in all athyreotic patients. PLoS One. 2011;6(8):4-10. https://doi.org/10.1371/journal.pone.0022552.
29. De Castro JPW, Fonseca TL, Ueta CB, et al. Differences in hypothalamic type 2 deiodinase ubiquitination explain localized sensitivity to thyroxine. J Clin Invest. 2015;125(2):769-81. https://doi.org/0.1172/JCI77588.
30. Hoermann R, Midgley JEM, Larisch R, Dietrich JW. Lessons from randomised clinical trials for triiodothyronine treatment of hypothyroidism: have they achieved their objectives? J Thyroid Res. 2018;2018:1-9. https://doi.org/10.1155/2018/3239197.
31. Wiersinga WM. T4 + T3 combination therapy: any progress? Endocrine. 2019;66(1):70-8. https://doi.org/10.1007/s12020-019-02052-2.
32. Gordon MB, Gordon MS. Variations in adequate levothyroxine replacement therapy in patients with different causes of hypothyroidism. Endocr Pract. 1999;5(5):233-8. https://doi.org/10.4158/EP.5.5.233.
33. Ojomo KA, Schneider DF, Reiher AE, et al. Using body mass index to predict optimal thyroid dosing after thyroidectomy. J Am Coll Surg. 2013;216(3):454-60. https://doi.org/10.1016/j.jamcollsurg.2012.12.002.
34. Roos A, Linn-Rasker SP, Van Domburg RT, Tijssen JP, Berghout A. The starting dose of levothyroxine in primary hypothyroidism treatment. Arch Intern Med. 2005;165(15):1714-20. https://doi.org/10.1001/archinte.165.15.1714.
35. Bach-Huynh TG, Nayak B, Loh J, Soldin S, Jonklaas J. Timing of levothyroxine administration affects serum thyrotropin concentration. J Clin Endocrinol Metab. 2009;94(10):3905-12. https://doi.org/10.1210/jc.2009-0860.
36. Skelin M, Lucijanić T, Liberati-Čizmek AM, et al. Effect of timing of levothyroxine administration on the treatment of hypothyroidism: a three-period crossover randomized study. Endocrine. 2018;432-9. https://doi.org/10.1007/s12020-018-1686-1.
37. Sawin CT, Geller A, Wolf, PA. et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older patients. New English J Med. 1994;331(19):1249-52. https://doi.org/10.1056/nejm199411103311901.
38. Chakera AJ, Pearce SHS, Vaidya B. Treatment for primary hypothyroidism: current approaches and future possibilities. Drug Des Devel Ther. 2012;6:1-11. https://doi.org/10.2147/DDDT.S12894.
39. De Escobar GM, Obregon MJ, Escobar del Rey F. Maternal thyroid hormones early in pregnancy and fetal brain development. Best Pract Res Clin Endocrinol Metab. 2004;18(2):225-48. https://doi.org/10.1016/j.beem.2004.03.012.
40. Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the infant. N Engl J Med. 1999;341(8):549-55. https://doi.org/10.1056/NEJM199908193410801.
41. Idris I, Srinivasan R, Simm A, Page RC. Maternal hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome. Clin Endocrinol. 2005;63(5):560-5. https://doi.org/10.1111/j.1365-2265.2005.02382.x.
42. Allan WC, Haddow JE, Palomaki GE, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. J Med Screen. 2000;7(3):127-30. https://doi.org/10.1136/jms.7.3.127.
43. Negro R, Schwartz A, Gismondi R, et al. Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. J Clin Endocrinol Metab. 2010;95(9):44-8. https://doi.org/10.1210/jc.2010-0340.
44. Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol. 2005;105(2):239-45. https://doi.org/10.1097/01.AOG.0000152345.99421.22.
45. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2012;97(8):2543-65. https://doi.org/10.1210/jc.2011-2803.
46. Ross DS. Hypothyroidism during pregnancy: clinical manifestations, diagnosis and treatment [Internet]. In: Cooper DS, Lockwood CJ, Mulder JE, editors. UpToDate; 2021. Available from: https://www.uptodate.com/contents/hypothyroidism-during-pregnancy-clinical-manifestations-diagnosis-and-treatment?sectionName=Preexisting%20treated%20hypothyroidism&search=hypothyroidismtreatment&topicRef=7855&anchor=H57693680&source=see_link#H57693673. Accessed 8 Apr 2021.
47. Arafah BM. Increased need for thyroxine during pregnancy in women with primary hypothyroidism. New English J Med. 2001;344(23):1743-9. https://doi.org/10.1056/nejm200106073442302.
48. Gaiser R. Timing and magnitude of increases in levothyroxine requirements during pregnancy in women with hypothyroidism. Surv Anesthesiol. 2005;49(1):15-16.

Etoricoxib

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Etoricoxib is an oral nonsteroidal anti-inflammatory drug (NSAID). It acts as a selective cyclo-oxygenase-2 (COX-2) inhibitor with anti-inflammatory, analgesic and antipyretic properties.[1,3] Etoricoxib is available as a tablet formulation in strengths of 60 mg, 90 mg or 120 mg.[1]

Indications

Etoricoxib is indicated for patients 16 years of age and older for the following:[1]

- Symptomatic relief of osteoarthritis (OA) and rheumatoid arthritis (RA).
- Treatment of:
  - ankylosing spondylitis (AS),
  - acute gouty arthritis,
  - primary dysmenorrhoea, and
  - moderate to severe acute postoperative pain associated with dental surgery.
- Short-term relief of acute pain, treatment limited to a maximum period of 8 days.

Dosing

Etoricoxib should be used for the shortest duration at the lowest effective daily dose and may be taken with or without meals. The table below outlines the recommended daily doses of etoricoxib by indication:[1]

Indication	Recommended dose*
Osteoarthritis	60 mg once daily
Rheumatoid arthritis	90 mg once daily
Ankylosing spondylitis	90 mg once daily
Short-term relief of acute pain	90 mg or up to 120 mg once daily limited to a maximum of 8 days treatment
Acute gouty arthritis	120 mg once daily limited to a maximum of 8 days treatment
Primary dysmenorrhoea	120 mg once daily
Postoperative dental pain	90 mg once daily

*Since doses exceeding the recommended doses for each indication have either not been studied or efficacy was not determined, doses should not exceed the recommended daily doses.[1]

Pharmacokinetics

Etoricoxib is well absorbed, reaching maximum plasma drug concentration levels after approximately one hour.[2,3] Data has indicated an absolute bioavailability of approximately 100% following oral administration.[3] Furthermore, studies have demonstrated that the pharmacokinetic properties of etoricoxib are not significantly affected by food.[1,2] Etoricoxib has a long half-life of approximately 22 hours, allowing for once-daily dosing.[1,2]

Efficacy

Postoperative dental pain: the analgesic effect of etoricoxib 90 mg was found to be superior to paracetamol/codeine 600 mg/60 mg and placebo, and similar to ibuprofen 600 mg as measured by total pain relief over the first 6 hours.[3] Compared to paracetamol/codeine 600 mg/60 mg and naproxen 550 mg, the analgesic effect of etoricoxib was similar to that of naproxen and both were superior to paracetamol/codeine 600 mg/60 mg.[2] Compared to paracetamol/oxycodone 650 mg/10 mg, etoricoxib demonstrated superior analgesic efficacy and less adverse events.[2]

Osteoarthritis: A placebo-controlled study demonstrated the maximum effective dose for the treatment of osteoarthritis as 60 mg of etoricoxib.[2,3] Improvement was seen from the second day of therapy and maintained for up to 52 weeks.[3] Compared to ibuprofen 50 mg three times a day, similar efficacy was demonstrated with etoricoxib, with patients in the etoricoxib group experiencing fewer gastrointestinal side effects.[2] Etoricoxib 60 mg and naproxen 500 mg (given twice daily) demonstrated similar efficacy in patients with knee or hip osteoarthritis.[2]

Rheumatoid arthritis: Etoricoxib 60 mg and 90 mg once daily both provided significant improvements in pain, inflammation, and mobility with these effects maintained over a 12-week period.[3] Etoricoxib 90 mg daily demonstrated comparable efficacy to that of naproxen 500 mg twice daily.[2]

Acute gouty arthritis: Etoricoxib 120 mg once daily for 8 days was found to be as effective as indomethacin 50 mg three times daily. Pain relief was observed within four hours after initiation of etoricoxib.[2,3]

Ankylosing spondylitis: Etoricoxib 90 mg once daily provided significant improvements in spine pain, inflammation, stiffness and function. Etoricoxib 60 mg daily and 90 mg daily demonstrated similar efficacy compared to naproxen 1 000 mg daily.[3] In a systematic review, etoricoxib was superior to celecoxib, ketoprofen and tenoxicam in pain reduction.[4]

Dysmenorrhoea: Etoricoxib 120 mg provided analgesic efficacy superior to placebo for total pain relief over 8 hours and similar total pain relief to that of naproxen sodium 550 mg for the treatment of dysmenorrhoea.[5]

The Oxford Pain Group League table of analgesic efficacy is based on information (numbers needed to treat [NNT]) from systematic reviews of randomised, double-blind, single-dose studies in patients with moderate to severe pain. NNT were calculated for the proportion of patients with at least 50% pain relief over 4–6 hours compared with placebo in randomised, double-blind, single-dose studies in patients with moderate to severe pain. Analgesic efficacy is expressed as the NNT, the number of patients who need to receive the active drug for one to achieve at least 50% relief of pain compared with placebo over a 4–6 hour treatment period. Etoricoxib demonstrated the lowest NNT, with 1.5 and 1.6 at doses of 180/240 mg and 120 mg, respectively.[6]

Safety of etoricoxib according to prescribing information

Precautions

- Etoricoxib may predispose patients to cardiovascular events, gastrointestinal events or cutaneous reactions.[1]
- Etoricoxib may cause hypertension to a greater extent than other NSAIDs and other selective COX-2 inhibitors. Therefore, blood pressure monitoring during treatment with etoricoxib is advised. Alternative treatment should be considered if there is a significant rise in blood pressure.[1]
- Etoricoxib may increase the risk of thrombotic events such as myocardial infarction and stroke.[1]

Drug interactions

Drug	Interacting effect	Points to consider
Ciclosporin and tacrolimus	Increase in the nephrotoxic effect of ciclosporin or tacrolimus	Renal function should be monitored
Warfarin	Approximate 13% increase in prothrombin time international normalised ratio (INR)	Standard monitoring of INR values should be conducted
Rifampicin	Significant decrease in etoricoxib plasma area under the curve (AUC)	
Methotrexate	Possible increase in methotrexate plasma concentrations and reduced renal clearance of methotrexate	Monitoring for methotrexate-related toxicity should be considered, when etoricoxib doses are over 90 mg daily and used concurrently with methotrexate
Diuretics Angiotensin converting enzyme (ACE) inhibitors Angiotensin receptor blockers (ARBs)	Possible reduction in antihypertensive effects	Monitor blood pressure; consider alternative treatment if blood pressure increase is significant
Lithium	Possible increase in plasma lithium levels	Monitoring of plasma lithium levels may be required
Aspirin	Increased risk of gastrointestinal ulceration	
Oral contraceptives	Increased incidence of adverse events associated with oral contraceptives	Consider venous thromboembolic events in women at risk
Hormone replacement therapy	Increase in oestrogen exposure which may increase the risk of adverse events associated with hormone replacement therapy	

Side effects

The most common side effects reported during clinical trials include: abdominal pain, flatulence, heartburn, diarrhoea, dyspepsia, epigastric pain, nausea, ecchymosis, flu-like symptoms, alveolar osteitis, oedema or fluid retention, dizziness, headache, palpitations, hypertension, increased ALT, AST levels.[1,3]

Comparative safety data

Results from a systematic review comparing the efficacy, safety and tolerability of diclofenac, ibuprofen, naproxen, celecoxib, and etoricoxib in patients with pain caused by OA or RA demonstrated:[7]

- Etoricoxib was associated with the lowest incidence of major upper gastrointestinal events compared to diclofenac, naproxen, ibuprofen and celecoxib.
- Risk of withdrawal of treatment (due to any cause) was lowest for etoricoxib.

Results from a meta-analysis showed that etoricoxib was not associated with an increased cardiovascular risk compared to placebo and naproxen, while celecoxib demonstrated an increased cardiovascular risk compared to placebo.[8]

The risk of thrombotic cardiovascular events of etoricoxib was compared to diclofenac. In a pooled analysis of data, patients received either etoricoxib (60 or 90 mg) or diclofenac (150 mg daily) for OA or RA. While results demonstrated similar efficacy and rates of thrombotic cardiovascular events for etoricoxib and diclofenac, etoricoxib was associated with a

S3

AZCURA

Etoricoxib 60mg I 90mg I 120mg

EXERCISE YOUR **RIGHT TO MOBILITY**

AZCURA is indicated for the symptomatic relief of:[1]

- osteoarthritis (OA)
- rheumatoid arthritis (RA)

AZCURA is indicated for the treatment of:

- ankylosing spondylitis (AS)

AZCURA is indicated for the short-term† treatment of:

- acute gouty arthritis (AGA)
- acute pain‡ (AP)
- acute post-operative dental surgery pain (APOP)
- primary dysmenorrhoea (PD)

†treatment limited to a maximum of 8 days treatment
‡acute pain affiliated to inflammation

References: 1. Azcura 60, 90, 120 Professional Information approved by SAHPRA, 30 June 2020.
S3 AZCURA 60 (film coated tablets). Each tablet contains 60 mg etoricoxib. Reg. No.: A47/3.1/0546. S3 AZCURA 90 (film coated tablets). Each tablet contains 90 mg etoricoxib. Reg. No.: A47/3.1/0547. S3 AZCURA 120 (film coated tablets). Each tablet contains 120 mg etoricoxib. Reg. No.: A47/3.1/0548. For full prescribing information refer to the approved package insert. Zydus Healthcare SA (Pty) Ltd, Block B, Southdowns Office Park, 22 Karee Street, Centurion, 0157. Tel. no.: +27 (0)12 748 6400. AZC/06/22/AD.

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more favourable gastrointestinal safety profile. Rates of upper gastrointestinal events were lower with etoricoxib than with diclofenac.[9]

Important prescribing points

- Etoricoxib may increase the risk of cardiovascular effects, which increase with dose and duration of exposure. Therefore, the shortest duration possible and the lowest effective daily dose should be used.[1]
- Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with etoricoxib after careful consideration.[1,3]
- Etoricoxib should not be used as a substitute for aspirin for cardiovascular prophylaxis because of its lack of effect on platelets.[1,3]
- Antacids do not have a clinically significant effect on the pharmacokinetics of etoricoxib.[1]

References

1. MSD (Pty) Ltd. Arcoxia®. South African Package Insert. 11 October 2013.
2. Takemoto JK, Reynolds JK, Remsberg CM, Vega-Villa KR, Davies NM. Clinical pharmacokinetic and pharmacodynamic profile of etoricoxib. Clin Pharmacokinet. 2008;47(11)703-20. https://doi.org/10.2165/00003088-200847110-00002.
3. Arcoxia® summary of product characteristics. Available from: https://www.medicines.org.uk/emc/medicine/29136.
4. Wang R, Dasgupta A, Ward MM. Comparative efficacy of non-steroidal anti-inflammatory drugs in ankylosing spondylitis: a Bayesian network meta-analysis of clinical trials. Ann Rheum Dis. 2016;75(6):1152-60. https://doi.org/10.1136/annrheumdis-2015-207677.
5. Malmstrom K, Kotey P, Cichanowitz N, Daniels S, Desjardins PJ. Analgesic efficacy of etoricoxib in primary dysmenorrhea: results of a randomized, controlled trial. Gynecol Obstet Invest. 2003;56(2):65-9. https://doi.org/10.1159/000072735.
6. Oxford League table of analgesics in acute pain. 2007. Available from: http://www.bandolier.org.uk/booth/painpag/Acutrev/Analgesics/Leagtab.html. Accessed 19 Jan 2017.
7. Van Walsem A, Pandhi S, Nixon RM, et al. Relative benefit-risk comparing diclofenac to other traditional non-steroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors in patients with osteoarthritis or rheumatoid arthritis: a network meta-analysis. Arthritis Res Ther. 2015;17(1):66. https://doi.org/10.1186/s13075-015-0554-0.
8. De Vecchis R, Baldi C, Di Biase G, et al. Cardiovascular risk associated with celecoxib or etoricoxib: a meta-analysis of randomized controlled trials which adopted comparison with placebo or naproxen. Minerva Cardioangiol. 2014;62(6):437-48.
9. Cannon CP, Curtis SP, FitzGerald GA, et al. Cardiovascular outcomes with etoricoxib and diclofenac in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) programme: a randomised comparison. Lancet. 2006;368(9549):1771-81. https://doi.org/10.1016/S0140-6736(06)69666-9.

It's a new dawn. It's a new day.

Kaajal Chetty

President, SAAHIP

Kaajal Chetty

I may be exaggerating when I say it feels like a post-apocalyptic world, but the COVID-19 pandemic has made us feel a cacophony of emotion. Not only have our personal lives been affected, but so too have our professional lives. No one prepared us to be soldiers in the battle against an invisible enemy. Armed with vaccines, handwashing and social distancing, we seem to be slowly taking control once again. Our nemeses (ignorance, vaccine hesitancy and Dr Social Media) do still conspire against us. We battle on.

During lockdowns, some families video-called often, keeping in touch more than they did pre-COVID. People learned to bake bread and find their inner gourmet chef.

Did you, the pharmacist, know where you fit in the situation? Juggling home, work, your mental and emotional well-being? Did you gain from your experiences? For many, their pharmacy family became their support system. We put our differences aside and found strength in each other to take home. We had to be strong for our families and stronger for our patients. We have experienced loss and tragedy but also witnessed miracles and heart-warming moments.

Often, it's been overwhelming and exhausting, and perhaps you've felt unappreciated. And if no one else has said it, or if you just need a reminder … Thank you! Thank you for being, for trying, for hanging in there. You are valued!

I know there are many pharmacists out there running on fumes, but just as our nation tries to regain her strength, so should you. Find your balance and make time for yourself. Rediscover what makes you happy. You've fought valiantly and deserve that medal of honour.

Whilst we master the technique of dividing our attention and energy on multiple issues, let us hope that we can bring more focus on matters relating to our profession. It is still within our reach to enhance and improve pharmacy. With the re-emergence of National Health Insurance planning, renewed emphasis on Antimicrobial Stewardship, discussion on pharmaceutical stock challenges, etc., we need to use all this newfound strength to take control of our professional future.

It certainly has been a challenging few years, but after all of this, you are here today with a chance to journey on. I am optimistic that together we can accomplish great things. Even if it means simplifying processes and working smarter, let us engage. Be proud of how far you've come and excited for how far you will go.

I hope you can close your eyes and sing along with me (and Michael Bublé), "It's a new life. For meeeee … And I'm feeling … Goooood!"

The South African Association of Hospital and Institutional Pharmacists (SAAHIP)

35th Annual Conference and 65th AGM
10–13 March 2022

It's our turn

Improving patient safety through excellence

Obey Madzingo

SAAHIP exco 2021/2022

Our very first virtual conference!

Of course, none of us saw this coming. As we bade farewell in Pretoria after the 34th annual conference, plans were already in motion for the 35th conference. Little did we know it would neither happen in 2021 nor would we see each other for the following two years. The pandemic threw numerous curveballs, but what remained was the willpower to showcase the work done by our institutional pharmacists. It was our turn to dance in the rain, adapt to change and continue to inspire the minds of our association.

As the organising committee, we had hoped to utilise all the lessons we learnt through organising conference at a completely new venue, for the upcoming conference, but alas, it wasn't meant to be! New skills had to be gathered all over again, technology took centre stage and needed to be embraced. Because we could not meet in person, the 2022 conference had to be virtual. The Whova app was used to host the conference. This came with its own perks too. The conference festivities started a month before the actual virtual one, for example, numerous competitions were run, and the conference was open to all SAAHIP members too. As soon as the conference went live, it was set abuzz by the attendees.

A multitude of discussion topics and groups sprouted daily. Data bundles also seemed to run out extremely fast. One had to go to bed late at night or wake up early in the morning to catch up on all the scintillating conversations. Some of the most popular discussion topics that emerged were:

- Emerging roles for pharmacists and the difference between pharmacists and clinical pharmacists
- COVID vaccine myths and hesitancy
- Pharmacy management hacks
- Medicine availability and national surveillance centre dashboard reporting
- Does a Master's in Pharmacy give you an edge?
- CCMDD
- Adjusting to life after COVID-19
- Bad experiences in the pharmacy
- Top two factors impeding efficient pharmaceutical services

Thanks to the organising committee, the most active people on the conference platform were rewarded. By the end of the virtual conference, the leaderboard had the following top three leading the pack:

1st	Thembie Siyaya – Mpumalanga Branch
2nd	Dr Sheshnee Moodley – Eastern Cape Branch
3rd	Nhlanhla Mafarafara – Limpopo Branch

The most popular photo, posted by Nondumiso Makwakwa from the Mpumalanga Branch, was a throwback from the 2018 conference

The most interesting caption was posted by Nhlanhla Mafarafara from the Limpopo Branch. It read: *"Fever is not a sign of ceftriaxone deficiency"*.

Two weeks before the date of the virtual conference, the first social event took place, i.e. Speed Networking. This event aimed to facilitate the attendees' meeting and interaction with as many new people as possible. All participants were placed on virtual tables in groups of three to four. They were then asked to play a game of two truths and a lie, and they were shuffled after every 5 minutes.

The organising committee ran a raffle for all the participants and the following prizes were awarded:

1st Thembie Siyaya – Mpumalanga Branch

2nd Bonolo Teki – Northern Cape/Free State Branch

3rd Renesha Bhikraj – KwaZulu-Natal Inland Branch

Just a week before the virtual conference, the second social event took place, i.e. the SAAHIP Quiz Night. Attendees were put in groups according to their University Alumni to battle it out. This was a heavily contested battle, but there was only one victor, the Rhodes University Team!!! The category that really separated the men from the boys was "SAAHIP's history". These questions were curated by Susan Buekes and by the end of the evening, everyone wished they had paid attention during the 2020 conference and read her blog too.

New leadership

Finally, the 65th AGM was upon us, and on 11 March 2022, the general council elected the new leadership as follows:

President
Kaajal Chetty

Vice President
Nhlanhla Mafarafara

Treasurer
Hannes Stegmann

Secretary
Obey Madzingo

Academic session

The academic session followed on 12 March 2022, where all presentations were done virtually. A new format had to be adopted – except for the Pearl presentations, all presentations followed the same format.

Awards

Life Health Care Award

The best virtual presentation award was won by Monet van Antwerpen. Monet also won the audience's favourite presentation award. Her presentation topic was "Warfarin toxicity from drug interactions".

The runner-up for the best virtual presentation award was Erin Watt, with the presentation of "Rational use of medicine in TB patients with adverse effects".

The Pearl Award

This award was won by Armand Algra. His topic was "Crap Happens: So let's have our Sh$@t together". You just had to be there! Armand also won the YPG joke contest award.

Membership Award

By a large margin, the branch with the most growth was Kwazulu-Natal Inland. They grew their membership by 82%.

In second place was North West with 21% growth.

In third place was KwaZulu-Natal Coastal with 20% growth.

Awards of Honour

For their tireless work on behalf of SAAHIP, the Association bestowed the Awards of Honour on two individuals.

Award of Honour – Susan Buekes

Tribute by Kaajal Chetty

Theodore Roosevelt once said, "The more you know about the past, the better prepared you are for the future."

It's hasn't been until recently that I have begun to understand this statement. The journey of SAAHIP through the decades has been a grand one. The foundations set by our predecessors are strong and have ultimately led to the committee's growth and success.

Having interacted with this award recipient over the past few years, I have grown to understand and appreciate her passion and drive. Her unwavering commitment to the profession, well after retirement. Really an inspiration in her own right!

It is my pleasure to acknowledge Susan Buekes as a recipient of a SAAHIP Award of Honour. Congratulations!

With a career spanning over 50 years, Susan has worked in various state and private hospitals, retail pharmacies, KZN DOH head office, and even as a junior lecturer at the then Natal School of Pharmacy. She has even practiced on different continents! She started in a small country hospital and retired while acting as head of pharmaceutical services ... such a journey!

Whilst a student, she was actively involved in the Natal Pharmaceutical Students' Association and served on the Branch committee. From 1979 to the present, she is actively involved in SAAHIP serving in various capacities on Branch Committees and on the National Executive Committee. In 1985, Susan was elected as Branch Chair of SAAHIP KZN Coastal. She was also the editor of FORUM, the national journal of the Association from 1980 to 1987. She is at present a member of the Pharmaceutical Society of South Africa and an active member of SAAHIP KZN Inland.

During the past twenty years, she has had many articles and letters published in the South African Pharmaceutical Journal, obituaries for deceased colleagues, as well as opinion pieces under the section "Nibbles".

Despite being retired from paid employment, she has maintained an interest in the profession. Throughout her life as a pharmacist, she has made it her business to submit comments that she had on draft legislation affecting pharmacy or her as a citizen. She still comments on proposed legislation. She still writes opinion pieces and letters when she feels strongly about events, good or bad, that affect the profession or her. She has also commented on the SAPC annual and financial reports.

We appreciate her efforts in compiling a narrative of our Association's history. It is no simple task. We are appreciative of her "keeping us on our toes" by trying to ensure that we always use best practices. For challenging and teaching us that we should never lose our passion and continue to fight for what's right. For helping us grow stronger as leaders.

I would like to end with an excerpt from the 1982 Chairman's Report written by Mr HM Jamnadas:

"This year we had 10 committee meetings. All of them, except one at Mrs Buekes residence at 41 St. Thomas Road, Durban. With the notice of one meeting we got written apologies from her children Deidre and Corolyn for making a noise. Such was the spirit of our meetings and I was very touched. Thank you, Sue, our editor an indispensable secretary. Your dedication despite your responsibilities is greatly appreciated."

Susan, just as you were honoured then, we would like to take this opportunity to honour you once again for your dedication and commitment to this Association! For always having the interest of the profession at heart. Heartiest congratulations to you!

Award of Honour – Nitsa Manolis

Tribute by Shawn Zeelie

Nitsa began her working career as a medical technologist in a clinical diagnostic laboratory, having completed her BTech in Biomedical Technology. Her focus was Haematology.

Her passion, however, was, and is, Ballroom and Latin American dancing, which is where she met Lorraine Osman. She soon went to work at the PSSA, where she got involved with the SA Pharmaceutical Journal. Her attention to detail made her the perfect person for proofreading – a new verb was born. Instead of "nitpicking" it was discovered that her

personal brand of "Nitsapicking" spotted grammatical, spelling and layout mistakes before the SAPJ goes to print.

In order to familiarise herself with pharmacy, Nitsa quietly went and spent her spare time acquiring another BTech degree, this time in pharmaceutical sciences.

It didn't stop there – Nitsa will always step in and help when someone is falling behind with their work. She gradually got more involved with administrative functions within the PSSA, and she is responsible for sending out newsletters on behalf of PSSA national, as well as for smaller branches of PSSA and SAAHIP. She also runs a tight ship when it comes to travel and accommodation arrangements for meetings.

Thank you, Nitsa, for all you have done and continue to do for SAAHIP.

Virtual exhibitors and sponsors

A special thanks to our colleagues from trade who continue to support our conferences even in the most difficult of times. It is indeed through their generosity that our conferences are possible.

- NovoNordisk
- PharmaDynamics
- Fresenius Kabi
- Government Employees Medical Scheme (GEMS)
- South African Health Products Regulatory Authority (SAHPRA)
- Life Health Care

Closing remarks

On behalf of the Mpumalanga Branch, we would like to extend our sincere gratitude to the members for all your support throughout our term as the conference organising committee. To the Southern Gauteng Branch, we wish you all the best of luck as you take over the reins as the incoming organising committee. The people have spoken, and we hope to have a physical conference in 2023!

The accidental pharmacist

Sham Moodley
Vice-Chair ICPA Board of Directors, Honorary Research Fellow School of Health Science, University of KwaZulu-Natal, South Africa
Corresponding author, email: fshamm@iafrica.com

Based on the keynote address presented at the 35th SAAHIP Conference, 2022.

Dr Sham Moodley

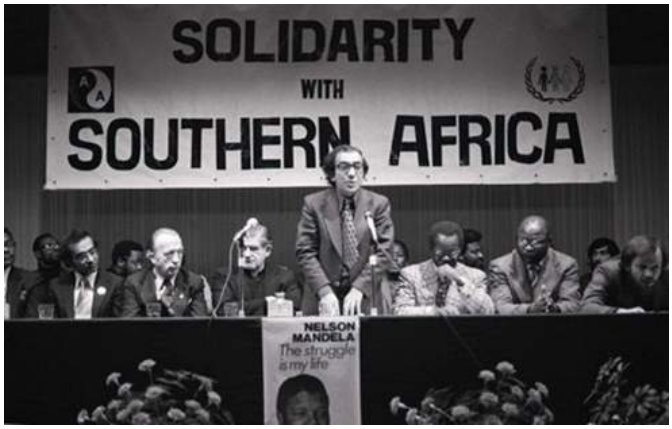
It was a huge privilege and honour to open the 35th Annual Conference. I must declare that this is one of the conferences I most enjoy attending, as it has consistently provided the perfect blend of learning, diversity, and networking. We must start by acknowledging and celebrating the incredible success story of pharmacy through the pandemic since March 2020, and specifically, the amazing work done in both the public and private sectors in leading the COVID-19 vaccine initiative. Pharmacists and their teams delivered in excess of 6.5 million doses of vaccine.

I was invited to tell my story of how I came to be where I am today. So let me start by declaring that I am an "accidental pharmacist", and then I will proceed to tell you why.

"Some people feel the rain. Others just get wet"

Bob Marley's last outdoor concert before his death at the age of 36 was at Dublin's Dalymount Park on Sunday 6 July 1980.[1] It was a sunny afternoon gig in which he referenced the Irish struggle for democracy and smoked his holy herb, before performing his very famous Redemption Song. Marley's writing, in lines such as *"Some people feel the rain, others just get wet",* profoundly impacted my attitude to life. It is a commentary not only about what you want, but what you are willing to DO to get there. Thankfully I continue to FEEL the rain. Other major influences include my parents, who risked sending an 18-year-old to study in Ireland in the Seventies. Ireland exposed me to a nation in the throes of their own violent revolution and the addictive passion of the likes of Bobby Sands, who gave his life for Irish freedom on 5 May 1981, following 66 days on a hunger strike.[2] I lived Ireland's history through their passionate rendition of revolutionary songs and stories of heroism and sacrifice.

I was privileged to be at the Irish Anti-Apartheid Movement Rally in 1979 to hear our very own son of South Africa, Oliver Reginald Tambo,



Irish Anti-Apartheid Movement Rally in 1979

talk about solidarity, unity of purpose and sacrifice.[3] I found myself moved and inspired and my own quest for justice and equity was born as I stood there, a young man born and raised in the womb of apartheid. I enrolled for a Bachelor of Science degree, majoring in Pharmacology. My home for 4 years was Melville House, built in 1778, now part of the beautiful University College Dublin campus.[4] Ireland provided the platform for the growth of my organisational skills through my involvement in the South African Student Association, where we hosted fund-raising concerts, debates, speakers like Kadar Asmal, Mac Maharaj and Oliver Tambo, and produced quarterly newsletters, and even played soccer on Sundays in the lower tier of the Irish league. We worked in the summer months to subsidise our incomes, cleaning hotel rooms and bussing restaurant tables. I even drove an ice cream truck in Kansas City, Missouri.

My exposure to these amazing experiences allowed me to grow and expand my horizons. The realisation emerged that "Change is possible". Those ideals ring true even now in the world of pharmacy. So, yes. 'It's our turn!' In order to achieve SAAHIP's goals – "to deliver excellent pharmaceutical services as an integral part of a multidisciplinary team, and to meet the emerging healthcare opportunities and challenges", we need:

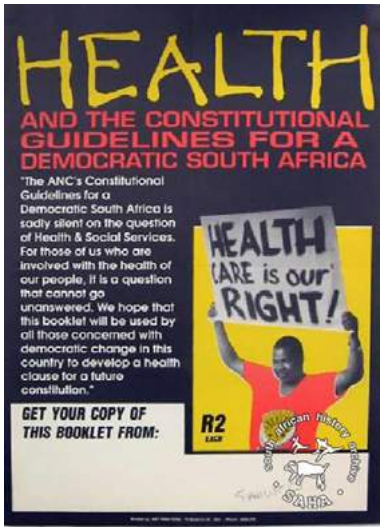
- unity of purpose;
- solidarity as a profession; and
- an inherent belief in justice and equity.

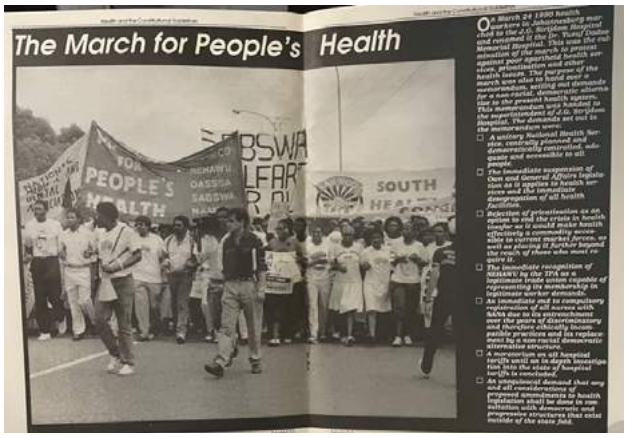
After graduation, I arrived home hoping to lecture in Pharmacology. Professor Virendra Rambiritch, whom some of you may know, indicated that I would have to wait for someone to die before I would be considered for a post. Instead he persuaded me to enrol for a place as a student in the School of Pharmacy. As my new journey began, I became what can only be described as "the accidental pharmacist".

Despite being enrolled as a full-time student, I functioned in reality as a part-time student. Part-time because the political candle that was lit in Ireland burnt brightly. Together with a few activists who had returned to the country, we founded the South African Health Workers Congress. That later evolved into the South African Health and Social Service Organisation (SAHSSO) in 1992. I honed my leadership skills in SAHWCO, spending my days in the lecture theatres, but most afternoons, nights and weekends in various portfolios within the SAHWCO Executive, as head of community projects, then editor of a progressive publication called *Health in the Hands of the People*, and in the unity forum that culminated in a national structure. My political exposure included being part of delegations that:

- consulted the exiled ANC Health Desk on South Africa's future health policy in 1987 (my final year);
- attended the International Labour Organization (ILO) policy conference on the health workforce in Southern Africa, held in Harare; and
- contributed to the guidelines that form the basis for the health-related rights enshrined in the Constitution.

While these exposures were truly an honour and a privilege, I have to admit that I barely made it out of Pharmacy School.





I worked in the public sector for 7 years before I left to open a pharmacy in the community in which I grew up, where I continue to practise today, after 29 years. In 2004, I received a call from the Pharmaceutical Society's President, Siddiq Tayob, to assist in opening the doors for talks with government. The rest is history. On that Easter Sunday, we had our first meeting with the then Minister of Health, Dr Manto Tshabalala-Msimang, in Pretoria. To stretch the analogies – in Irish history, this could be equated to either the Easter Uprising of 1916, where independent pharmacy rose to the fore, or Michael Collin's 1920 Bloody Sunday, with Ivan Kotzé and I still struggling to get the dispensing fee right. So my leadership roots also emanate from my deep commitment to social justice, equality and equity.

My academic journey, too, evolved in response to new challenges that emerged within the health sector. I registered for a post-graduate diploma as well as a Master's in HIV and AIDS Management in 2003 and 2005, respectively, at Stellenbosch University. This helped me to contribute to pharmacy's strategic approach to the HIV pandemic. More recently, two important changes in legislation that had a huge impact on medicine availability have demanded an informed response from Pharmacy: the single exit price and the question of pharmacy ownership. Apart from my involvement in structures that took on this battle, I also embarked on my PhD, to study the impact of such legislation both on the profession as well as on the patient, which I completed in 2020. I was able to publish three papers on this subject in peer-reviewed journals.[5-7] This endeavour enabled me to contribute significantly to the body of scientific evidence necessary to advance pharmacy. I hope this motivates each of you to engage in similar initiatives to advance our profession in an informed way. Remember: 'It's our turn'.

That, in a nutshell, satisfies the brief I was given to tell part of my story. Against this backdrop, allow me to focus the next part of my talk on the direction I believe pharmacy leaders should steer this ship. I firmly believe that the International Pharmaceutical Federation (FIP) Development Goals provide a perfect framework within which to contextualise priorities for pharmacy over the next decade.[8] These goals should serve as a basis for investment in pharmacy by government and funding authorities, as well as for the planning and delivery of policy initiatives to transform pimary health care (PHC). They are aligned to the United Nation's Sustainable Development Goals (SDGs).[9] Having these common goals across all sectors will allow us to develop a unified and sustainable vision for pharmaceutical services in South Africa and the drive towards universal health coverage (UHC). As the hospital sector, I am sure that you are familiar with the widely-published Basel Statements on the Future of Hospital Pharmacy.[10] Andy Gray referenced this well when he received the Donald E Francke Medal in 2015.[11] He aptly outlined the concept of a shared vision and a bottom-up approach that dictates a willingness to participate and a refusal to accept the *status quo*. There is an excellent online self-assessment tool that allows you to measure your hospital's services against the Basel Statements.[12] If we apply this assessment across our provincial hospitals, we could find pockets of excellence, duplicate those experiences, and highlight the barriers to the delivery of a first-class pharmaceutical service.

Evidence-based clinical pharmacy has become the key narrative across the world. Non-adherence, untimely use of medicines, antibiotic

overuse, medication errors, suboptimal use of generic medicines and mismanaged polypharmacy account for almost US$500bn of avoidable costs.[13] Good-quality pharmacy research that gets the right answers hinges on the right patients, the right intervention and the right outcomes. This, I believe, is the future of our profession. There is no doubt that utilising the expertise of a pharmacist in any setting can transform all of the markers outlined above. Ross Tsuyuki, a pharmacist and professor of medicine at the University of Alberta, Canada, has become a Twitter favourite of mine. His published research indicates that pharmacy-managed hypertension achieves better outcomes and costs less than 'usual care'.[14] In a series of controlled studies, pharmacists demonstrated their effectiveness in managing hypertension, diabetes and dyslipidaemias. These separate threads were pulled together in the REACH study, which involved 723 patients. A 21% relative risk reduction in cardiovascular risk (owing to improved adherence) was shown, and previously undiagnosed chronic kidney disease was identified in 113 patients. Tsuyuki emphasised that all of this work was done WITHIN the existing framework of pharmaceutical services, confirming that such initiatives are both sustainable and reproducible. Two important, local hospital-based studies have further highlighted the potential role of the pharmacist. The first, by Annor et al. found 5 300 potential drug-drug interactions (DDIs) among 500 patients aged 65 and older prescribed five or more medicines with an average of 10 DDIs per patient.[15] More recently, in January 2022, Bojuwoye et al. demonstrated a high level of polypharmacy, especially in those over 60 years of age.[16] These patients were prescribed an average of 12.1 different medicines, and were exposed to a potential 10.3 DDIs.

We have a huge ethical and professional responsibility as pharmacists to NOT turn a blind eye and to treat this phenomenon with the seriousness it warrants. I have a vision of SAAHIP driving and demanding a solution in the interest of our patients. Potential resources could include reliable, regularly updated clinical decision support systems as well as information technology such as a computerised drug interactions checker. These should be vital accessories to assist the pharmacist in every sector to help identify, monitor and prevent dangerous drug combinations being prescribed to our patients. To reach their full potential pharmacists must practise at the top of their licensure by expanding their services from traditional dispensing to chronic disease management, point-of-care testing, patient education, and medication therapy management to achieve desired clinical outcomes. Even though pharmacists possess an expert body of medication knowledge, the application of this knowledge in practice is not standardised, nor is it embedded in a consistent manner across the profession. Healthcare systems are increasingly focused on health outcomes and quality measures, and the need for pharmacists as integral members of the healthcare team has never been greater. I believe that focusing on the following three areas will benefit the profession:

- a *philosophy of practice*, which is the ethical foundation that prescribes appropriate professional behaviour;
- a *patient care process*, to organise the knowledge and decisions that need to be made and the actions that need to be taken; and
- a *practice management system*, which would accommodate service delivery that assures quality, accountability, outcomes, and payment to sustain the long-term viability of the practice.

Most care pathways stop at the prescribing step and fail to articulate patient outcomes. By contrast, under the proposed National Health Insurance (NHI) contracting scheme, health care providers will be reimbursed based on the services they provide, the outcomes achieved, and their impact on the health of the population. If pharmaceutical services are not clearly defined, costed correctly and can show impact, the necessary funding for such services will not flow from NHI. It is therefore imperative that the pharmacy profession determine what these services will be, how they will be costed, and how outcomes and impacts will be measured. A vision for the future really centres around three significant gaps in health and well-being, care and quality, and funding. Appropriate preventive initiatives are needed for chronic non-communicable diseases, but financial investment is needed to develop new care and quality models.

The COVID-19 pandemic has highlighted the differential risks in our unequal society, served by an unequal healthcare system even after 27 years of democracy. Risks vary for the rural vs the urban, the women and girls vs everyone else, those in poverty vs the affluent, the compromised vs the healthy. The pressure on the hospital sector has been immense. Many young pharmacists had to grow up overnight and take responsibility for life-changing decisions. We commend them for that. To continue to elevate the profession, pharmacists must get involved beyond the dispensing windows. Active involvement in our organisations is critical. Perhaps the most vital lesson is that of the importance of collaboration. Working with trusted partners, hospital pharmacies can solve today's problems and explore new opportunities, ensuring a bright future for pharmacy after COVID-19.

References

1. Mallin E. Bob Marley. Dublin 6 July 6 1980. Rootfire, 2015. Available from: https://root-fire.net/bob-marley-dublin-july-6-1980/.
2. Taylor P. Bobby Sands: The hunger strike that changed the course of N Ireland's conflict. BBC News, 1 May 2021. Available from: https://www.bbc.com/news/stories-56937259.
3. Tambo O. Statement by Oliver Tambo at the freedom rally organised by the Irish Anti-Apartheid Movement, 26 January 1979. Available from: https://www.sahistory.org.za/

References available on request.

Patient encounters … Pharmacists have rights too!

Gary Black
(Dip.Pharm) FPS

Introduction

While pharmacists strive to act in the best interests of their patients through their professional practice of pharmaceutical care, they are often subject to abuse by unreasonable, angry patients. Such patients are quick to claim their right to healthcare as specified in the Patient's Rights Charter but slow to accept their own responsibilities with regards to respect for pharmacists, or their use of medicine and the healthcare system.

Some common scenarios

Pharmacists working in both public and private community pharmacies will be familiar with at least one or more of the scenarios listed below:

- Patients who, after spending hours waiting to see a doctor, complain bitterly and rudely when having to wait for their prescription to be dispensed.
- Patients who are clearly misusing S5 psychiatric medication and who become loud and abusive when questioned about early repeats, the need to provide a new prescription, and/or when such early refill claims are rejected by their medical aid.
- Patients presenting fraudulent prescriptions.
- Patients requesting medicines such as antibiotics, cortisone, etc., without prescription … *" because I know my condition and I have had it before, why must I pay to see a doctor just for a script, why can't you just give it to me?!"*
- Patients who falsely accuse pharmacist's assistants or pharmacists of being "difficult" or rude when they are questioned about their constant requests for potentially addictive S2 medicine, especially pain medication containing codeine.

Often, under the circumstances described above, the patient becomes loud and abusive, making a public display of their anger in some vain hope that this will embarrass the pharmacist into acceding to their demands. Furthermore, such patients are quick to air their grievances on public media platforms such as Facebook or lay complaints with the Pharmacy Council or senior management of the pharmacy. Many such complaints cannot be substantiated, and it has been shown that some such patients even tell blatant lies.

Patient's rights and responsibilities

The Patient's Rights Charter clearly spells out both patient's rights and responsibilities and pharmacies are required to display posters of these rights and responsibilities in an area where they can be easily read by patients. Whilst we fully respect the **patient's rights** including access to healthcare, dignity and confidentiality, we must point out that patients also have a number of **responsibilities**, especially:

- *To respect the rights of other patients, health workers and health care providers.*
- *To utilise the health care system optimally and not to abuse it.*

In terms of the National Health Act, *Section **19 – Duties of users,*** patients must:

- *adhere to the rules of the health establishment when receiving treatment or using health services at the health establishment;*
- *treat health care providers and health workers with dignity and respect; and*
- *a health care provider may refuse to treat a user who is physically or verbally abusive or who sexually harasses him or her.*

Furthermore, the National Health Act, in terms of Section ***20. Rights of health care personnel,*** clause (4) specifies; **a *health care provider may refuse to treat a user who is physically or verbally abusive or who sexually harasses him or her.***

Pharmacist's fundamental responsibilities and rights

Section 22 of the **Bill of Rights** provides for every citizen to practice their profession freely, subject to the laws regulating that profession. Pharmacists have fundamental responsibilities, built on principles embodied in the **Pharmacist's Oath**, and the **Code of Conduct**. Their prime concern must be the welfare of the patient and they are expected to practice pharmaceutical care subject to Good Pharmacy Practice Rules, the Pharmacy Act, the Medicines and Related Substances Act and all other laws and regulations governing the practice of pharmacy.

To fulfil these responsibilities, pharmacists should exercise the following fundamental rights:

- *To practice pharmacy in the best interest of patient and community health and well-being.*
- *To exercise professional judgment within their scope of practice when delivering care to patients.*
- *To be treated in a considerate, respectful, and professional manner by patients and supported by employers and supervisors.*
- *To a workplace free of racism, discrimination, bullying, or harassment, as well as physical, verbal, or emotional abuse.*

For a pharmacist to act professionally in practicing pharmaceutical care and maintain dignity in exercising his rights in the face of dissatisfied, abusive patients is often far easier said than done!

What to do about it

Here are some suggestions on how to create conditions conducive to positive interaction with patients, avoid conflict situations, and deal with complaints satisfactorily.

Prevention is better than cure

- Create conditions conducive to good pharmacist/patient interaction. Reconsider the physical layout of the pharmacy to ensure easy access, good signage, comfortable and inviting waiting areas and adequate areas for privacy/confidentiality for counselling of patients.
- Re-examine the workflow of the dispensary. If possible, reorganise stock for quick, easy access while dispensing and organise staff to work in efficient teams to speed up the dispensing process safely with accurate checking. All this may be done to minimise waiting times. If a prescription is going to take some time to prepare, warn the patient about the delay and keep them informed on the progress of the process.
- Have sufficient, suitably qualified staff to cope with the workload. This requirement will vary, depending on the nature of dispensing being done and the profile of patients being served. All staff must be well trained, work according to appropriate SOPs and the workload organised in such a way as to enable maximum time to be spent on interaction with patients.
- Be supportive of junior staff, encourage referrals to more experienced colleagues, especially when encountering difficult patients, or unusual/complicated requests and prescriptions.
- Be consistent in how you treat patients and in fulfilling your ethical and legal obligations in controlling and recording the sale of medicine.
- Educate patients on their rights and responsibilities regarding their prescriptions, responsible use of medicine, access to PIT and self-care. Have the Patient's Rights and Responsibilities posters in place and clearly visible to the patients, use instructive videos in the waiting area, have sufficient, appropriate information pamphlets available and make responsible use of social media.

Address problems speedily, professionally, in a positive, friendly and helpful spirit

- Develop a practical SOP for complaint procedures. Train all staff in its implementation and be consistent in its application.
- Staff should be trained in recognising potential conflict situations, how to handle such problems and correctly refer to more experienced colleagues.
- Record all incidents accurately for future reference in any enquiry or for use as examples in training.
- Encourage patient feedback, asking questions such as: *Were you treated in a friendly, professional manner; Did you receive adequate advice on the correct use of the medicine provided; Have you any suggestions on how we could improve your experience in our pharmacy; Did you receive the pharmaceutical care you expected?*

When all else fails

- If, at any stage, a patient becomes aggressive or abusive, refer the matter to a senior, experienced pharmacist immediately. The patient should be spoken to confidentially in a private area.
- Every attempt should be made to resolve the conflict. However, if the patient has behaved aggressively and abusively, it must be made clear to such a patient that their conduct in the pharmacy is unacceptable and the reasons clearly spelt out.
- If there are sound grounds for discontinuing service to the patient, the reasons for doing so must be made clear and the patient must be referred to another pharmacy, with their repeat prescription, if necessary.
- If the patient shows remorse and is prepared to change, give them another chance, but make it clear that any repeated poor behaviour will result in refusal of service.
- Carefully record the incident, with signed affidavits from fellow staff. Follow the correct protocols in reporting the incident to senior management.

Conclusion

Patients visiting a pharmacy are usually not their normal selves. They are often feeling ill and miserable or could be upset and concerned about a loved one or friend on whose behalf they are coming to obtain medicine. So, while pharmacists and their staff should be aware of this and strive to treat all patients equitably, with respect and dignity in applying pharmaceutical care, they must be wary of potential abusive patients. *You cannot please all the people all the time! But, if patients are abusive, dishonest or disrespectful, just remember,* ***pharmacists have rights too!***

This document is a guideline and does not necessarily reflect official policy of the Pharmaceutical Society of SA. Any member wishing to implement proposals made in this document, must do so in accordance with the requirements of the Pharmacy Act 53 of 1974, Medicines & Related Substances Act 101 of 1965 and all other relevant legislation, and, if necessary, should seek legal advice to ensure compliance.

For further information and copies of reference documents, please contact the author: gary@pssacwp.co.za

Bibliography

- Patient's Rights Charter
- The National Health Act, Act 61 2003
- Constitution of Republic of South Africa, Chapter 2, Bill of Rights
- The Pharmacist's Oath (PSSA)
- BN 108 of 2008 Rules relating to Code of Conduct
- APHA Pharmacist's fundamental Rights and Responsibilities
- Sample SOP available on request

gsk

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References: **1**. Centers for Disease Control and Prevention. Micronutrient Facts. Available at: https://www.cdc.gov/nutrition/micronutrient-malnutrition/micronutrients/index.html. Accessed 27 June 2021. **2**. World Health Organization. Micronutrients. Available at: https://www.who.int/health-topics/micronutrients#tab=tab_1. Accessed 27 June 2021. **3**. Blumberg JB, Frei BB and Fulgoni VL, *et al*. Impact of Frequency of Multi-Vitamin/Multi-Mineral Supplement Intake on Nutritional Adequacy and Nutrient Deficiencies in U.S. Adults. *Nutrients*. 2017;9(8):849. **4**. Shakoor H, Feehan J and Al Dhaheri AS, *et al*. Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? *Maturitas*. 2021;143:1-9. **5**. Centrum Adult Informations Leaflet. **6**. Data on file ID no: 3998.