May/June 2024. Vol 91 No 3
SA Pharmaceutical Journal

sapj

ISSN: 2221-5875

loss of hearing in the affected ear [1]

vomiting [1]

headaches [1]

vertigo [1]

sweating [1]

nausea [1]

loss of balance [1]

vomiting [1]

aural fullness in the affected ear [1]

tinnitus in the affected ear [1]

vertigo [1]

headaches [1]

REVIHIST 24 mg is indicated for the symptomatic treatment of **vertigo** associated with Meniere's Syndrome.[2]

Slow the dizziness

with

S3 revihist 24 mg
betahistine dihydrochloride

Usual daily dose:
24 mg to 48 mg in divided doses.[2]

References: 1. Martel J (medically reviewed by Han S). Meniere's Disease. Healthline Media [Internet]. 2018 September. Available from: https://www.healthline.com/health/menieres-disease [cited: 02 March 2023]. **2.** REVIHIST 24 mg Professional Information July 2022. S3 **REVIHIST 24 mg.** Reg. No.: 52/5.6/1028. Each tablet contains 24 mg betahistine dihydrochloride. For full prescribing information refer to the professional information approved by SAHPRA (07/2022). Accord Healthcare (Pty) Ltd. Reg. No.: 2004/011257/07. Building 2, Tuscany Office Park, 6 Coombe Place, Rivonia, 2128, Gauteng, South Africa. Postnet Suite 182, Private Bag X51, Rivonia, 2128. Tel: +27 11 234 5701/2/3, Fax: +27 11 234 5700, Customer Care No.: +27 11 234 5950. Email: medinfo@accordhealth.co.za. REV/004/MAY23/ADb.

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incorporating
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- South African Association of Community Pharmacist Sector of the PSSA
- SA Association of Hospital and Institutional Pharmacists
- SA Association of Pharmacists in Industry

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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

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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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5. Follow the five steps to submit your paper.

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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Editorial

Pharmacists are indispensable healthcare providers and are essential to the success of the NHI system

Natalie Schellack
Editor: SA Pharmaceutical Journal

The recent implementation of the National Health Insurance (NHI) Act and the amendments to the Mid-Level Worker Regulations present both challenges and opportunities for pharmacists to adapt and thrive in the evolving healthcare landscape.

The NHI Act, signed into law in May 2024, aims to achieve universal health coverage for all South African residents. This landmark legislation will require pharmacists working in both public and private sectors to register with the NHI Fund, adhere to its regulations, and adapt to new payment structures for the provision of pharmaceutical care. Pharmacists will play a crucial role in the successful rollout of the NHI, dispensing medications, providing patient education, and ensuring the appropriate use of medicines by NHI beneficiaries. The NHI's focus on integrated and coordinated care will necessitate the development of new collaborative practice models and the enhancement of pharmacists' clinical skills and expertise.[1–4]

The South African Pharmacy Council (SAPC) has published amendments to the Mid-Level Worker Regulations, set to be implemented in April 2024.[5] These changes establish a clear career path for pharmacy support personnel and introduce the Pharmacy Technician qualification. The Pharmacist's Assistant (Basic) and Pharmacist's Assistant (Post-Basic) qualifications have been registered on the Occupational Qualifications Sub-Framework (OQSF), allowing progression from Basic to Post-Basic level and potentially to the Pharmacy Technician qualification.[5] Pharmacy technicians can provide technical support in dispensing prescriptions and selling Schedule 0, 1, and 2 medicines under pharmacist supervision.[5] The new Mid-Level Worker Regulations provide new opportunities for collaborative practice models within the pharmacy.

The implementation of the NHI Act and the amendments to the Mid-Level Worker Regulations presents both challenges and opportunities for pharmacists in South Africa. Including potentially increased responsibilities and scope of practice for pharmacists, changes to reimbursement models, and the need for enhanced coordination and collaboration with other healthcare providers. This now also paves the way for significant opportunities, such as expanded roles for pharmacists in patient-centred care, increased recognition of pharmacists' expertise, and the potential for innovative service delivery models.

In this edition, we are excited to introduce the success story of a pharmacist with less than five years of experience, as well as invite pharmacists to share their thoughts and experiences. We encourage all pharmacists, regardless of their practice setting, to contribute their unique perspectives and insights. Please send us your contributions on the SAPJ platform https://ojs.sabinet.co.za/index.php/sapj/about/submissions.

The date is drawing near for the 82nd FIP World Congress of Pharmacy and Pharmaceutical Sciences that will be held in Cape Town, South Africa, from September 1st to 4th, 2024. This presents an opportunity for South African pharmacists to engage with their global counterparts, learn about the latest advancements in the profession, and contribute to shaping the future of pharmacy. Do not forget to register https://fip.eventsair.com/cape-town-2024/lp/Site/Register.

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3. Minister Joe Phaahla: President's signing of National Health Insurance Bill. (2024, May 15). Available from: https://www.gov.za/news/speeches/minister-joe-phaahla-president%E2%80%99s-signing-national-health-insurance-bill-15-may-2024.
4. The role of medical schemes once the NHI is implemented - Discovery. (n.d.). Available from: https://www.discovery.co.za/corporate/health-nhi-the-role-of-medical-schemes.
5. South African Pharmacy Council. (2024) Pharmacy Act (53/1974). Regulations relating to the registration of persons and the maintenance of registers.Amendment Regulations, 2024. Government Gazette No. 50528, 19 April. Available from: https://www.pharmcouncil.co.za/Media/Default/Board%20Notices/Regulations%20practice%20of%20pharmacy_Amendment2024.pdf. Accessed 1 July 2024.

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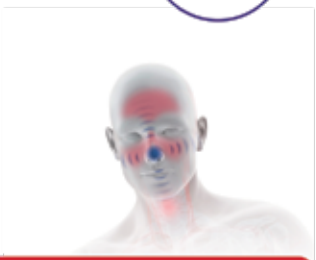

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President's Message

Focussing on the future

Tshifhiwa Rabali
PSSA President

Being around for more than 75 years is a huge achievement for the Pharmaceutical Society of South Africa. The Society is 78 years old this year and so much has been achieved, however there is still much to be done.

The Society will have to refocus its energies and engage with stakeholders who did not have a working relationship previously with the Society. Our participation with other forums on the African continent will have to be revived. The PSSA is already a member of the African Pharmaceutical Forum and regular meetings with them will be sought so that we can understand their challenges and they can also understand ours. The PSSA is also a member of the Commonwealth Pharmacists Association and our engagement with them will have to be revived.

National Health Insurance Bill

The PSSA has observed the signing of the National Health Insurance Bill into law and will keep monitoring its implementation so that pharmacists are not left behind in this endeavour of the government to address health inequalities. Our engagement with the Department of Health will be prioritised so that we are part of the implementation of NHI`s phases.

Unemployed pharmacists, community service pharmacists (CSPs) and interns

These issues were addressed with the Deputy Director General of Health (Dr Percy Mahlati), the Chief Director at the department (Dr Luvuyo Bayeni) and their team in April 2024. It was a very cordial meeting where I re-introduced the PSSA to the Department of Health as the Society that represents more than 13 000 pharmacists and pharmacy personnel and it is on a transformative drive. They mentioned that the issue of unemployed pharmacists/interns is receiving attention as they have requested funding from Treasury. They have also approached the provinces to see if there are any vacancies and funding available.

With regards to the community service pharmacists' programme, the reply received was that currently the programme will continue as it is, but that discussions will take place in the 2025/2026 financial year as to whether the CSP programme is still viable in its current format.

PSSA branches

Our branches are being encouraged to hold more CPDs, webinars, symposiums and workshops so that they can attract more pharmacists to become members of the PSSA. The process of reviving inactive branches is ongoing. Branches play a crucial role in the recruitment of new members and the National Office will continue to support them in doing that.

Legacy projects

Our involvement with the hosting of the FIP 2024 Congress has encouraged us to look into the legacy projects that the PSSA can be proud of in future. This will be a milestone achievement that the PSSA would have undertaken during its existence.

Lastly, I would like to thank you all for the good work that you continue doing in providing pharmaceutical services to the citizens of this country.

I thank you.

82nd World Congress on Pharmacy and Pharmaceutical Sciences in Cape Town, South Africa 1 to 4 September 2024

The programme for the 82nd World Congress was published online in April 2024 (https://capetown2024.fip.org/programme-overview/). It was developed with the congress theme of "Innovating for the future of pharmacy" in mind. In the previous issue of the SAPJ, the theme and the three subthemes focusing on equitable healthcare, drug innovations, and artificial intelligence (AI) were explained in detail. In this issue, readers are informed on what to expect from the academic programme at Congress.

Pre-congress events

Before the official opening of the Congress, participants are invited to explore the unique learning opportunities in the pre-congress symposiums. These will take place on Saturday, 31 August, and Sunday, 1 September, and offer a deep dive into the most pressing topics in our field.

- The FIP Digital Pharmacy Summit (Saturday, 31 August, from 9 am to 5 pm) is designed to equip pharmacists with the necessary skills to leverage technology for health promotion, disease prevention, and medication optimisation. This includes understanding the impact of technology and digital health on healthcare and pharmacy practices, identifying the opportunities and risks of AI in pharmacy, and recognising the importance of comprehensive education and training for building trust in AI-driven operations. Register on the online portal at R2 100 per person to secure your spot at this transformative Summit.
- The Industry Pharmacy Section (IPS) workshop, in collaboration with USP (Saturday 31 August 2024, 9 am to 5 pm), is a must-attend for those interested in the latest innovations in pharmaceutical manufacturing technologies and their implications for Good Manufacturing Practices (GMP). In today's rapidly evolving pharmaceutical landscape, this knowledge is crucial for maintaining competitiveness and ensuring regulatory compliance. Register on the online portal at R2 600 per person for FIP members and R3 800 for FIP non-members to secure your seat for this insightful workshop.
- The Leadership Development Workshop (LDW) (Saturday, 31 August 2024, 9 am to 5 pm and Sunday, 1 September 2024, 9 am to noon) invites all Early Career Pharmaceutical Group (ECPG) and International Pharmaceutical Student Federation (IPSF) members to apply to attend the LDW in Cape Town. The workshop is designed to help build and develop leadership skills for early carer pharmacists, pharmaceutical scientists, and students that they can use in future endeavours. Applications for this event closed on 1 June 2024.
- The FIP Global Academic Leaders Forum (Sunday, 1 September 2024, from 9 am to 12:30 pm is an open event for academic pharmacy leaders (Deans, Heads of Schools, and School Directors) of Academic Institution Members (AIM) of FIP.

Sunday 1 September 2024

As we kick off our celebrations of Pharmacy Month 2024, we are also eagerly anticipating the arrival of Spring Day, which will add a touch of excitement and engagement to our event. Although the congress venue will be open for participants to collect registration badges, even if they are not attending any pre-congress events, it is vital to note that no lunch will be provided on this day to congress participants.

From noon to 1 pm, a First Timers session will be hosted, specifically for Congress participants attending the World Congress for the first time. At this session, the International Pharmaceutical Federation (FIP) will explain the Federation's vision and mission and elaborate on the structure and objectives the Federation aims to achieve. This event is an opportunity to meet other first-timers, FIP officials and FIP staff. This session is free to attend by all who, for the first time, attends an FIP World Congress.

All congress participants will be able to learn more about pharmacy in South Africa between 1 pm and 2:30 pm. This session, organised by the Cape Western Province Branch of the PSSA, will provide attendees with a snapshot of the different sectors, roles, positions, and settings pharmacists and pharmacy support personnel could perform in their scope of practice. Although the session is aimed at international participants visiting South Africa, locals are welcomed for moral support.

The official opening of the congress commences at 3 pm. The programme usually includes welcome addresses by the FIP President and other High Officials from the host country or province. Several awards and recognitions are also presented during this prestigious event. The dress code for this event is formal business attire (suit and tie) or traditional.

Following the opening ceremony is a welcome reception for all attendees in the Exhibition area, where light snacks and drinks will be served. This is the first view at the exhibition and an opportunity

to catch up with long-distance friends, visit exhibitors, build new networks or make new friends.

Academic programme on Monday, Tuesday, and Wednesday (2-4 September 2024)

Each morning will start with an early morning session from 8 am. During these sessions, Member Organisations (like PSSA) will have the opportunity to share ideas with one another. At these sessions, countries will describe their leading projects, share pioneering initiatives, specify the challenges pharmacists face in different settings, express ideas about advancing pharmacy to a global audience or share ideas in a global network.

At 9 am, the formal academic day will commence with a Plenary session aligned with one of the congress's sub-themes. Topics include equitable quality healthcare, the AI revolution, and sustainability. At each of these 90-minute sessions, a number of high-level and world-class expert speakers will paint a diverse picture on the topic so that participants have a holistic understanding of pharmacy's role in each.

A coffee and tea break will allow participants to enjoy complimentary refreshments in the exhibition area. It is also an ideal time to view the poster presentations from around the world, identify potential collaborations, or learn things to take back to their own practice settings.

From 11 am, participants will have to choose among seven parallel sessions which one to attend. Among the choices are four sessions that align with one of the congress sub-themes, namely equity quality, drug discovery or AI; a dedicated science-based session; a locally influenced session; or a session referred to as a Rapid-fire session, which is a selection of short oral presentations from abstracts received. At each of these 90-minute sessions, experts will share their knowledge with attendees on the session topic. Look out for the South African experts taking the stage.

During the 2-hour lunch break, lunch will be served in the exhibition area, and participants will have time to network, build relationships, and visit the exhibitors and poster presenters. In addition, several lunchtime symposiums will be offered, which participants can attend. Sponsors organise these sessions on specific topics relating to the pharmacy profession.

The afternoon parallel session again spoils participants with seven options to broaden their knowledge and expand their skills.

Following the afternoon coffee and tea break from 4 pm to 4:30 pm, the academic day will conclude with a plenary session linked with the congress sub-themes. Topics such as innovative drug discovery, patient partnerships in universal health coverage, and a concluding session on the future of healthcare, will bring the academic programme to a close.

Post-congress events

Although the Congress formally concludes on 4 September, participants could opt to join several events on Thursday, 5 September.

- An Educators' Summit focussing on responding to a call for innovation in pharmacy education and training (Thursday, 5 September 2024, from 9 am to noon) invites all academicians, educators, trainers, preceptors, and mentors to celebrate the education sector and discuss important determinants of pharmacy education with a community of international colleagues. Participants will be able to explore the issues and challenges relating to undergraduate and postgraduate education and continuing professional development, share solutions, introduce innovations and understand new educational guidelines and goals. Interested participants should register to attend via the online registration portal at R510 per person.
- The Cape Western Province Branch of the PSSA is organising Professional Tours (Thursday, 5 September 2024, 9 am to 3 pm) to various sector settings. There will be four tours focusing on visits to community pharmacies, hospital pharmacies, the pharmaceutical industry, and academia, respectively. Each tour will visit three facilities to showcase the sector's diversity. After the site visits, all tours will end at Pharmacy House, the branch office building, for a late lunch and visit to the museum, after which participants will be transported back to the CTICC. Although these tours are aimed at international participants, South African colleagues are also welcome to book through the online platform. The cost for the full-day tour is 60 euros (around R1 300) and includes a T-shirt. More detail is available on the congress website at https://capetown2024.fip.org/professional-tours-thursday-05-september-2024/.

PSSA members are reminded to make the most of this event being hosted in South Africa. Attend with an eager open mind to learn from others, share your insights and dream together about the prosperous future of pharmacy.

Social events with networking opportunities

During the Congress event, there are numerous social events and gatherings, which are ideal opportunities to network and build relationships with like-minded colleagues. For the full list of social events, please visit the official congress website at https://capetown2024.fip.org/programme/social-events/ or refer back to the January/February 2024 issue of the SAPJ.

The PSSA/Alpha Pharm distance learning programme 2024

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, 2024 – Eczema – New Insights

Eczema imposes a considerable burden on and substantially impairs the quality of life of patients and their families.

Eczema occurs most frequently in children but also affects adults. It is often associated with a personal or family history of atopy, which is a group of disorders that include eczema, asthma, and allergic rhinitis, also referred to as the "atopic triad". Several studies have linked the incidence and severity of eczema during childhood with later development of allergic rhinitis and asthma.

This module reviews the current information on eczema, its causes, and approaches to management.

The pharmacist is in an ideal position to provide patients with information on proper preventative skincare and can counsel patients on the appropriate management and treatment of their eczema.

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 2024 for pharmacy staff

The PSSA/Alpha Pharm pharmacy staff clinical education programme continues to offer front-shop assistants or pharmacists' 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, 2024 – Eczema

Eczema is a skin problem that causes dry, itchy, scaly, and red skin. It is the most common skin disorder in children and causes tremendous suffering to the child and his/her caregivers.

Eczema occurs most frequently in children but can also affect adults. It is estimated that up to 1 in 5 children and 1 in 20 adults may be affected by eczema at some point.

This module looks at eczema, its causes, symptoms, prevention, and treatment, and outlines the role of the Front Shop Pharmacy Staff in helping patients with eczema.

Eczema affects the quality of life of patients and their caregivers. Itching can be intolerable and affect sleep, and the need to apply emollients regularly can become a burden, particularly during symptom-free periods.

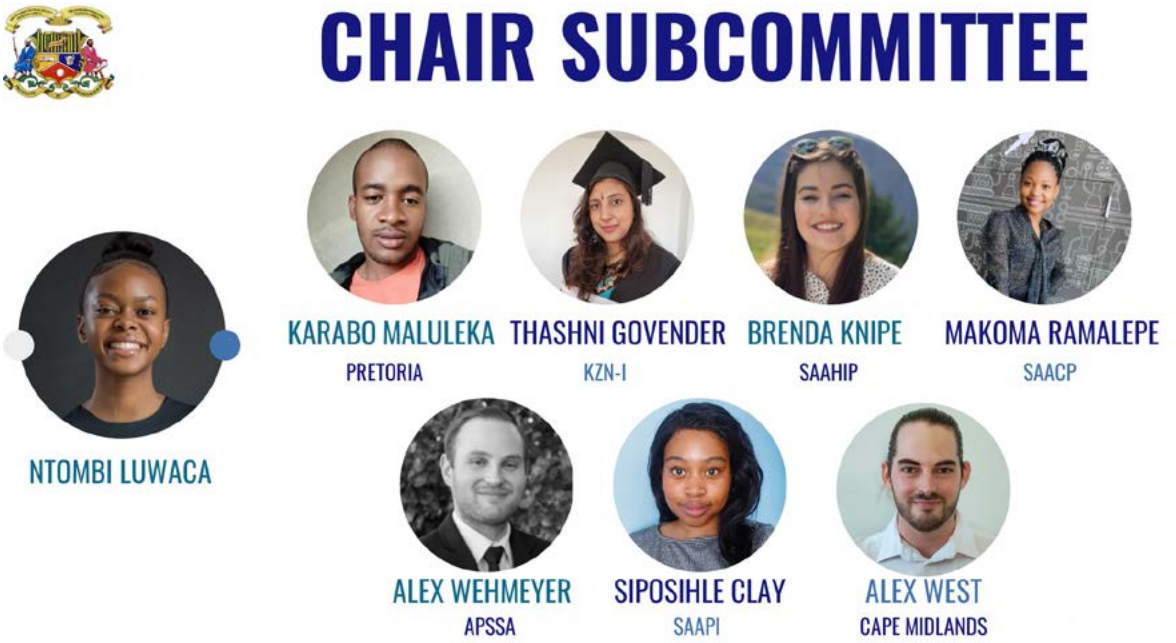
The Front Shop member of staff in the pharmacy can play a valuable role in assisting patients living with eczema and their caregivers.

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.

PSSA YPG's first-ever subcommittee

As the Steering Committee of 2023/24 comes to the end of its term, it is only fitting to permanently celebrate one of its biggest achievements, the first-ever PSSA YPG Subcommittee. This is a dynamic group of young people who are dedicated to serving the world of pharmacy and healthcare. The PSSA YPG Steering Committee thanks each and every one of them for their efforts, willingness to volunteer, and dedication to the projects of the PSSA.

Get ready world, a new team of brilliant minds is at your service!



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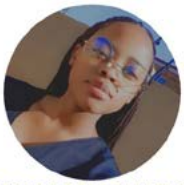

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  FIP ECPG, Member Relations Coordinator
- Handsome Mashego
  SAAHIP Mpumalanga Branch, Treasurer General
- Solofelang Matshidiso
  North West Provincial Branch, Young pharmacist representative on the ExCo

Au revoir: Until we meet again!

The voluntary responsibility to represent young pharmacists nationwide will never be an easy one, especially when one is also young and still in need of extensive training. We hope that the activities we planned throughout our term served some kind of purpose to your journey in the profession. Au revoir!

Feel free to reach out to us at
Email: ypg@pssa.org.za
Facebook: Young Pharmacists' Group of PSSA
Instagram: @pssaypg
Young pharmacists – connected, engaged, empowered and inspired!

Management of allergy and sinusitis

N Shirindza, E Bronkhorst

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Corresponding author, email: nkhensani.shirindza@smu.ac.za

Abstract

Allergic diseases are inflammatory disorders that occur chronically because of immune system activation by environmental factors or allergens. They are classified as type I hypersensitivity reactions mediated by Immunoglobulin E (IgE) antibodies. Atopy refers to the increased sensitivity of IgE antibodies to a specific antigen, with genetic predisposition being one of the risk factors. The clinical relationship between allergy and rhinosinusitis is not clear; however, rhinosinusitis is a result of the inflammation of the sinus mucosa due to the presence of an allergen, and it is either acute or chronic. Rhinosinusitis is, therefore, recognised as an inflammatory disorder of the paranasal sinuses and the nasal cavity. Acute rhinosinusitis (ARS) is usually caused by a viral infection, whereas chronic rhinosinusitis (CRS) is an inflammatory disorder with increased expression of cytokines. Treatments are aimed at reducing mucosal inflammation, thinning and clearing mucus, controlling infection, and treating symptoms such as nasal congestion, rhinorrhoea, sneezing and nasal itching. The goal of this article is to outline the current management approach for rhinosinusitis and review new treatment options and therapeutic techniques.

Keywords: allergy, sinusitis, inflammatory disorders

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Introduction

Allergic diseases are a group of chronic, systemic, inflammatory disorders that occur because of the immune system's excessive activation by certain environmental factors, also known as allergens. Allergens are grouped into chemical allergens, such as dyes; food allergens, such as nuts; and aeroallergens, such as pollen.[1,2,3] This type I hypersensitivity reaction is specifically mediated by the humoral immune system in which an allergen or antigen binds to allergen-specific immunoglobulin E (IgE) on the surface of mast cells. This binding results in the release of inflammatory mediators such as histamine.[2-6] Allergic diseases are known to be complex because, additionally, they can occur because of genetic predisposition, in which IgE antibodies have increased sensitivity to a specific antigen and are produced in response to minor exposure to environmental chemicals that would not be a trigger under normal circumstances. This is referred to as atopy.[1,2] During pregnancy or early childhood, environmental factors can alter the physiologic, immune, structural, and behavioural development and, therefore, alter the response patterns and create susceptibility to future diseases. Other than genetic predisposition, atopy risk factors include decreased exposure to infections and endotoxins, postnatal antibiotic use, air pollutants, exposure to allergens, gestational use of antibiotics and maternal stress.[3,4] Complex interactions between genetic and environmental factors result in different allergic diseases, such as allergic rhinitis, allergic asthma, atopic dermatitis, food allergy, and eczema, which also exist. Other common allergic conditions globally include rhinosinusitis, allergic conjunctivitis, and allergic oesophagitis. The prevalence of allergic diseases is on the rise, affecting 30% to 40% of the world's population. According to the World Health Organization (WHO), allergic diseases are among the top three disorders to be prevented and controlled in the 21st century.[4,7]

Pathophysiology of allergy and symptoms

The early and late phases of an allergic response

The body's response to an allergen occurs in two phases, i.e. the early and late phases. The presence of an allergen attracts antigen-presenting cells (APCs), such as dendritic cells found on the mucosal surface. The dendritic cells process and present peptides from allergens on the major histocompatibility complex (MHC) class II molecule, forming a complex. This complex forms a ligand for Naïve $CD4^+$ T-cell receptors and, once attached, differentiates the Naïve $CD4^+$ T-cells to activated allergen-specific Th2-cell. Th2-cells are responsible for the secretion of several cytokines, such as IL-4 and IL-5, which stimulate B cells to produce specific IgE antibodies and stimulate the proliferation of eosinophils, mast cells and neutrophils. The resultant antigen-specific IgE binds to high-affinity Fc receptors for IgE on mast cells or basophils.[8,9] The cross-linking of these receptors on mast cells causes the release of inflammatory mediators such as histamine, prostaglandins, and leukotrienes, which cause vascular leakage, bronchoconstriction, inflammation and intestinal hypermotility. These inflammatory mediators induce mucosal oedema and watery rhinorrhoea by causing blood vessels to leak.[9,10] Histamine activates H_1-receptors on sensory nerve endings, causing sneezing and pruritis. Histamine further exacerbates symptoms in what is called reflex secretory response by interacting with H_1 and H_2 receptors on mucosal blood vessels, leading to vascular engorgement (nasal congestion) and plasma leakage.[9] The early phase presents the rapid onset of acute symptoms such as itching, sneezing and rhinorrhoea, which develop within less than 20–30 min after allergic exposure.[11] The mediators further play a role in the late reaction, which occurs 4–6 hours after allergen exposure and subsides slowly. In this phase, eosinophil chemotaxis triggered by cytokines occurs, where several inflammatory cells, including eosinophils, migrate

to the nasal mucosa, breaking up and remodelling normal nasal tissue, resulting in nasal mucosal inflammation and obstruction. The schematic representation of the pathophysiology of allergic rhinitis is illustrated in Figure 1.[8-10]

Allergy and sinusitis

Sinusitis or rhinosinusitis is defined as a symptomatic inflammatory condition involving the paranasal sinuses and the nasal cavity.[12,13] The condition is classified as acute, sub-acute and chronic based on the duration. Acute rhinosinusitis (ARS) lasts up to four weeks, sub-acute rhinosinusitis lasts between 4–12 weeks and chronic rhinosinusitis (CRS) for more than 12 weeks. ARS is mainly due to bacterial, fungal, or viral infections, as well as allergens or exposure to inhaled irritants. It presents with common symptoms such as purulent nasal drainage accompanied by nasal obstruction and/or facial pressure pain. Other symptoms associated with ARS, which are not required for diagnosis, include malaise, reduced sense of smell, maxillary pain, and increased ear pressure.[4,12] CRS symptoms overlap with other conditions, especially allergic conditions, such as allergic rhinitis, and therefore, differential diagnosis is essential. Although extensively studied, the clinical relationship between allergy and rhinosinusitis is unclear.[14,15] In some studies, the cause-and-effect was proposed as the relationship between allergy and chronic sinusitis; however, in one study, the mention of systemic involvement in allergic reactions rather than local involvement provides insight into the mechanism underlying allergy and rhinosinusitis. Allergens can mostly not cross into the paranasal sinuses; however, once inhaled, the T-cell immune response is initiated.[16,15,17] The resultant inflammation of the sinus mucosa due to the presence of an allergen is also referred to as allergic rhinosinusitis, which can be either acute or chronic. The inability of the nose to eliminate the allergen results in an environment of chronic inflammation.[4] It has become accepted that chronic inflammatory processes play a role in the occurrence and development of chronic sinusitis, and unlike ARS, the aetiology of CRS displays more complex characteristics of inflammation.[4,13,15] Notably, patients who have CRS present with persistently inflamed mucous membranes, irrespective of the actual presence of allergens in the nasal cavity.[16] CRS is characterised by the type of inflammation, Type 2 (IL-5 and IL-13), Type 1 (IFN-γ) and Type 3 (IL-17A) and is further subdivided into three types, namely CRS without nasal polyps (CRSsNP), CRS with nasal polyps (CRSwNP) and allergic fungal rhinosinusitis.[18] The contribution of type 1 and type 3 inflammation to CRS is not understood. Majority of CRS especially CRSwNP exhibit type 2 inflammation.[18,19,20] There are other causes that play a role in the pathogenesis of rhinosinusitis, such as epithelial tissue hypersensitivity, disruptions of innate immunity and, the presence of bacterial colonisation and biofilm, and genetic and environmental factors. Inflammation is a common denominator for these various causes. Therefore, allergies such as allergic rhinitis may produce rhinosinusitis, supported by the fact that 25–58% of people with rhinosinusitis have some form of inhaled allergen sensitisation. Allergy may also exacerbate CRS by adding to the existing inflammation. This theory is encouraged

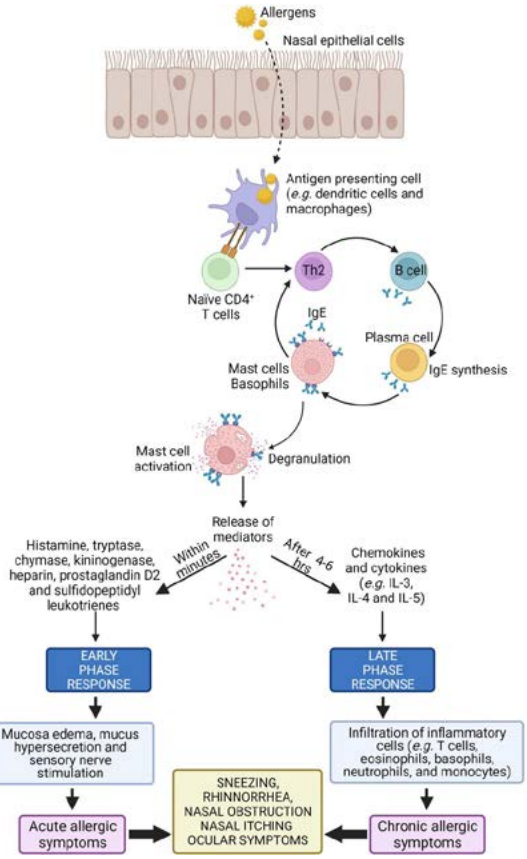

Figure 1: Schematic presentation of the pathophysiology of AR.[9]

by the fact that in CRS, the cell surface adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1) and other chemotactic molecules are expressed in abundance and have been assumed to form a part of the mechanism by which AR mediates CRS. In a study involving mice, hyper-responsiveness to histamine was demonstrated in a mice model of acute bacterial sinusitis where sinusitis was enhanced during exposure to aeroallergens.[20] Staphylococcus species found in the nose and paranasal sinuses can create a biofilm that becomes a source of superantigen and inflammation regardless of their inactive biofilm state. The superantigens further exacerbate the inflammatory response by triggering IL-4, IL-13 and TH2 cytokines that lead to IgE in the sinus tissues.[16,20] The resultant inflammation further prevents the clearance of bacteria from the sinus cavity, which may lead to the development of secondary bacterial sinusitis.[4,16]

Management of rhinosinusitis

Intranasal saline irrigation

Hypertonic intranasal saline irrigation is recommended for the supportive treatment of CRS due to its minor adverse effects, although irritation of nasal mucosa and burning sensation may occur.[12,21] The hypertonic solution, compared to the isotonic solution, proved to be superior in thinning and clearing mucus. Saline irrigation is expected to have anti-inflammatory effects and plays a role in removing inflammatory mediators such as histamine and prostaglandins. Moreover, saline irrigation directly

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- Always administer with milk or food.
- Always take the lowest possible dose for the shortest possible duration.

Adults & children 12+ years[1]

- 1 – 2 tablets every 4 – 6 hours.
- Do not exceed 6 tablets within a 24-hour period.

12s

24s

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Children 2–6 years[2]

5 mL once daily OR
2,5 mL twice daily

Children 6–12 years[2]

10 mL once daily OR
5 mL twice daily

Adults & children 12+ years[2]

10 mL once daily

150 mL

60 mL

Children 6–12 years[3]

1 tablet daily OR
half a tablet twice daily

Adults 12+ years[3]

1 tablet daily

30s

10s

WHY RECOMMEND FEXO?

Fexo is an effective antihistamine that provides relief of runny nose, itchy, watery eyes, sneezing and skin hives. It is available in two strengths without a prescription. Its non-drowsy formulation starts to relieve symptoms within one hour and lasts for up to 24 hours. Plus, it is suitable for adults and children 12 years and older[4].

Adults 12+ years[4]

1 tablet daily

10s

FEXO 120 is indicated for the relief of seasonal allergic rhinitis (SAR) symptoms[4].

30s

FEXO 180 is indicated for the relief of chronic idiopathic urticaria (CIU) symptoms[4].

S2 Reg. No. A40/5.8/0218. Ibumax Cold and Flu (Film-coated tablets). Each film-coated tablet contains Ibuprofen 200 mg and Pseudoephedrine HCl 30 mg.
S2 Reg. No. 37/5.7.1/0153. NS1 06/5.7.1/0093 (Namibia). S2 BOT0801310 (Botswana). Allecet Syrup. Each 1 mL of Allecet Syrup contains Cetirizine dihydrochloride 1 mg.
S2 Reg. No. 37/5.7.1/0034. NS1 06/5.7.1/0100 (Namibia). S3 BOT1001640 (Botswana) Allecet (Tablets). Each film-coated Allecet tablet contains Cetirizine dihydrochloride 10 mg.
S1 Reg. No. A38/5.7.1/0414, 0415. Fexo 120; 180. Fexo 120: Each coated tablet contains Fexofenadine HCl 120 mg. Fexo 180: Each coated tablet contains Fexofenadine HCl 180 mg.
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cleans the mucus to prevent bacterial growth.[13,21] It provides symptomatic relief from nasal congestion, rhinorrhoea, cough, and headache and prevents the condition from worsening.[12,21,22] Saline irrigations are affordable and can be administered at home.[21] In various guidelines, nasal irrigation is encouraged as a first-line treatment to avoid the overuse of antibiotics for CRS. Additionally, nasal irrigation promotes wound recovery in the nasal cavity and sinuses post-endoscopic sinus surgery (ESS), further preventing the use of unnecessary drugs post-surgery. The limitation to saline irrigation is the indirect flow as opposed to directly penetrating the sinuses, considering the complex structure of the sinuses with its various connections.[13]

Corticosteroid therapy

Intranasal (topical) corticosteroids are beneficial in both ARS and CRS.[12,23,24] They have proven efficacy in the treatment of allergic rhinitis as well as all forms of CRS, especially CRSwNP.[18,19] Corticosteroids suppress type 2 inflammation, which is typical of CRS. The suppression of type 2 inflammation results in the suppression of eosinophils and Th2-cells. The mechanism of action of corticosteroids involves the attenuation of the expression and release of pro-inflammatory cytokines from airway epithelial cells, therefore reducing inflammatory mediators and immunoreactive cells. Topical corticosteroid nasal sprays are recommended to prevent the recurrence of small to medium nasal polyps, although not always effective. In most cases, they are beneficial for the rhinitis symptoms.[19,25] The limitation to intranasal corticosteroids is the inconsistent nasal distribution in the presence of severe nasal mucosal oedema or large nasal polyps.[26] The inconsistent distribution is also because most formulations are low-volume devices (i.e. spray bottles), which do not provide an effective spray to penetrate sinuses optimally, especially ethmoids (Figure 2).[27] The solution to this could be the use of large-volume devices such as nasal irrigation or the change in position of the low-volume devices to maximise penetration. Although large-volume devices improve sinusitis nasal symptoms, the long-term safety has not been evaluated further.[18,26] Examples of intranasal corticosteroids include beclomethasone, budesonide, fluticasone, mometasone, triamcinolone and ciclesonide. The newer agents, i.e. mometasone, fluticasone and ciclesonide, have minimal systemic effects. Corticosteroids are effective at recommended doses without adrenal suppressive effects.[12,18,25] They are intended for short-term use to avoid adverse effects associated with long-term use, such as atrophy of the nasal mucosa.[4,25] The most common local side effects experienced with intranasal corticosteroids include nasal irritation or burning, stinging, dryness and crusting, and epistaxis. Oral or systemic corticosteroids can be used, as a brief course of 10-15 days, to shrink nasal polyps and may also be used in allergic fungal sinusitis. They are considered in cases of severe CRS when rapid symptomatic relief is needed (i.e. CRS flare-ups or in the postoperative period after sinus surgery).[26] In such instances, a tapered regimen of oral steroids is preferred. Oral corticosteroids include hydrocortisone, cortisone acetate, prednisone, prednisolone, and methylprednisolone.[28,29] Although

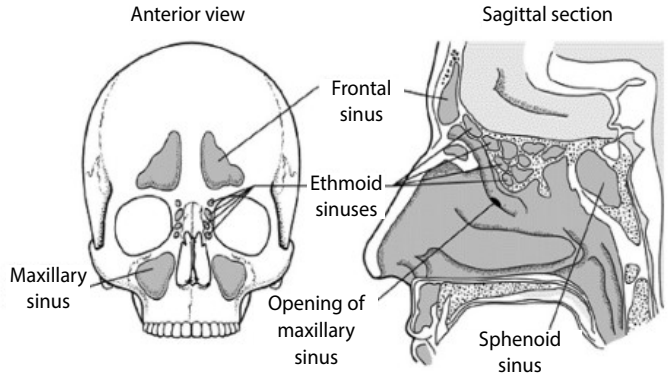

Figure 2: Anatomy of the paranasal sinuses.[27]

the combination of long-term decongestants with intranasal corticosteroids for CRS requires additional investigation, it is believed that topical decongestants may enhance the delivery of intranasal corticosteroids even in the presence of mucosal oedema.[30]

Decongestants (local and systemic)

Decongestants in rhinosinusitis are used for the relief of nasal congestion caused by mucosal oedema and local vasodilation, but there is little evidence in their role with regards to the quicker resolution of rhinosinusitis. Belonging to the drug class α-adrenergic agonist, decongestants relieve nasal congestion by inducing the release of norepinephrine from sympathetic nerves leading to nasal vasoconstriction. Topical decongestants improve acute symptoms in patients with rhinosinusitis but may reduce mucosal blood flow, which may increase inflammation and increase ciliary loss. The most used topical decongestants include xylometazoline, phenylephrine and oxymetazoline. Topical decongestants should not be used for longer than 3–5 days to avoid undesirable effects such as rhinitis medicamentosa.[4,25,30] Systemic decongestants include direct-acting (phenylephrine) and indirect-acting (pseudoephedrine). They are often combined with antihistamines, especially older generation H1-antihistamine, in preparations which may cause drowsiness and a lack of motor coordination. Their general non-selectivity results in other α-adrenoceptor stimulating effects not limited to the nasal cavity, such as hypertension, insomnia, and appetite suppression.[4,12]

Antihistamines

Although not indicated for use in bacterial ARS, antihistamines are first-line therapy for ARS with underlying allergic rhinitis.[12,25,31,32] Antihistamines are divided into first-generation and second-generation antihistamines and exert their action by competitive inhibition of the histamine receptors on airway mucosal cells. Second-generation antihistamines include cetirizine and levocetirizine, loratadine, desloratadine, ebastine, fexofenadine and mizolastine and have a higher affinity for histamine receptors with less sedating anticholinergic effects as compared to the first-generation antihistamines that cross the blood-brain barrier. First-generation antihistamines include promethazine, chlorpheniramine, dexchlorpheniramine and cyclizine.[4] They

are the most effective in atopic patients with symptoms such as rhinorrhoea, sneezing and nasal itching, which shows an improvement in sneezing after 14 days and have modest effects on nasal congestion, with improvement showing after 28 days. The use of antihistamines over a long time is more beneficial and effective than on-demand therapy.[12,31,33] All H1 antihistamines have anti-inflammatory properties due to their inhibition of the synthesis of the histamine-activated NF-κB, a transcription factor involved in the synthesis of pro-inflammatory cytokines and adhesion molecules. The effect is evident when taken on a regular daily dosing schedule rather than on an as-needed basis.[12] However, they can cause excessive drying, which can cause thickening of mucus and, therefore, impair mucus clearance. Therefore, there is no sufficient evidence to support the use of oral or intranasal antihistamines in both ARS and CRS.[25,26,34]

The leukotriene receptor antagonists

Examples of leukotriene receptor antagonists include zafirlukast and montelukast.[4] Montelukast is the only orally active leukotriene receptor antagonist that is approved for the treatment of allergic rhinitis.[12,25] It acts by binding to the leukotriene-1 receptor with high affinity and selectivity, thereby inhibiting the physiologic actions of leukotrienes in the upper respiratory system. It also reduces the number of eosinophils and, therefore, acts on a systemic level to reduce allergic inflammation. The evidence to support leukotriene receptor antagonists in the treatment of CRSwNS is moderate, especially when combined with topical or oral corticosteroids.[25,35] Montelukast is also available as a sprinkle and a chewable tablet for use in paediatrics[4] but is not currently registered as an over-the-counter drug for allergic rhinitis and rhinosinusitis because of the neuropsychiatric adverse effects associated with the drug such as depression, aggression, insomnia, irritability, and nightmares that were reported post-marketing.[36]

Immunotherapy/Monoclonal Biologic Therapies

This includes agents such as omalizumab (anti-IgE), reslizumab (anti-IL-5), mepolizumab (anti-IL-5) and dupilumab (anti-IL-4Rα).[37] A summary of the biologic medications is shown in Table I. Immunotherapy is only indicated, as an adjunct, in patients with moderate to severe refractory allergic rhinitis and CRS.[18,26] In South Africa, the only monoclonal IgE antibody registered is the subcutaneous omalizumab. Omalizumab works by binding to high levels of circulating, allergy-associated IgE antibodies and removes them from the circulation, thereby inhibiting the antibodies' ability to cause mast cell degranulation and subsequent allergic reactions.[12] Based on data from various studies, one study being a meta-analysis comparing IgE therapy to placebo in subjects with CRSwNP, there is a potential clinical efficacy of omalizumab for CRSwNP, favouring those with comorbid asthma.[18,38]

Antibiotics

Antibacterial agents in CRS are used to treat acute bacterial exacerbations where purulence draining from the sinuses is identified and are often prescribed in combination with topical nasal steroids and other adjuvant therapies.[18,25] Experts say that antibiotics used in CRS should have a broad spectrum. Antibiotics used for acute and CRS include amoxicillin-clavulanic acid, erythromycin, clindamycin, levofloxacin and ciprofloxacin or moxifloxacin, cefuroxime, doxycycline, co-trimoxazole for a duration of 10–14 days. Short-term antibiotic therapy (up to seven days) has a similar efficacy and outcome as long-term therapy (≥ 2 days longer than short-term) and has the benefits of less antibiotic-associated side effects.[12,25,39] However, there is inconclusive evidence for the optimal duration of therapy, most clinicians can prescribe from seven days to four weeks.[26] Evidence based on a 2016 Cochrane review of a limited number of placebo-controlled trials shows that there could be benefits with long-term antibiotic therapy especially for type 3 inflammation.[13,18] The general approach is to continue antibiotics until the patient is asymptomatic and has no mucopurulent discharge.[18] Amoxicillin is considered the first-line treatment in acute and CRS because of its favourable side effect profile. Monotherapy is sufficient in low-risk patients, but the combination with clavulanic acid is recommended in children, the elderly and patients who are more likely to have bacterial resistance, e.g. patients who were recently treated with antibiotics. Macrolides or fluoroquinolones are preferred in penicillin-allergic patients.[18,25] According to a survey, 94% of otolaryngologists prescribed oral antibiotics for CRS.[25] The limitation to antibacterial prescribing for acute and CRS, even with demonstrated efficacy, is the rise in resistant organisms. Bacteria cultured from purulence in CRS demonstrated resistance as compared with ARS. Therefore, according to antimicrobial stewardship the use of antibiotics should be only if necessary.[12,13]

Conclusion

Rhinosinusitis remains a prevalent disease and has a significant

Table I: Biologic Medications Approved or Being Evaluated for CRSwNP.[16]

	Dupilumab	Omalizumab	Mepolizumab	Benralizumab
Pharmacology	Fully human monoclonal anti-IL-4 alpha subunit antibody	Recombinant humanised monoclonal anti-IgE antibody	Recombinant humanised monoclonal anti-IL-5 antibody	Recombinant humanised monoclonal anti-IL-5 receptor alpha subunit antibody
Indication	Moderate to severe asthma with eosinophilic phenotype or with oral corticosteroid dependent asthma, atopic dermatitis, CRSwNP	Moderate to severe asthma with positive allergy testing, chronic urticaria	Severe asthma with eosinophilic phenotype, eosinophilic granulomatosis with polyangiitis	Severe asthma with eosinophilic phenotype

impact on overall quality of life. In this article, difference between acute and CRS were summarised and the fact that allergic rhinitis and rhinosinusitis are two distinct conditions that usually overlap and can coexist in a patient were highlighted. The management was discussed; the different available drugs and their mechanisms to improve overall disease prognosis. The current available treatments aim to reduce inflammation, which is a main cause of rhinosinusitis. Advancements in therapy, such an immunological therapy have significantly improved the management of rhinosinusitis patients and help reduce morbidity. Further evidence-based research must be done to encourage some of the recommended treatment options.

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Malaria in children: current approaches to treatment and prevention

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Abstract

Malaria remains a global healthcare challenge, especially in children under the age of five, who continue to be disproportionately affected. Clinical presentation of malaria is non-specific, ranging from flu-like symptoms in mild cases to multi-organ failure in severe cases. Prompt diagnosis and treatment determine case outcomes. Patient and caregiver education about malaria prevention is the cornerstone of malaria management and requires an individualised approach. As the seasonal transmission of malaria in South Africa starts waning towards May and rising again in October, it is essential that healthcare workers be informed about the latest prevention and treatment strategies.

Keywords: malaria, paediatrics, treatment, prevention, chemoprophylaxis

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Introduction

Malaria is a global preventable infectious disease that continues to be a major cause of illness and death.[1,2] According to the World Health Organization (WHO), there were approximately 249 million cases and 613 000 deaths in 2022.[3] Progress against the disease has largely been halted by the COVID-19 pandemic, with an increase of approximately 5 million cases and 55 000 deaths compared to 2021.[3] In sub-Saharan Africa (SSA), children under the age of five years old contribute to more than two-thirds of all malaria-related deaths.[3–5] This roughly translates to one death occurring every minute.[5]

Malaria transmission: South Africa

Malaria transmission in South Africa primarily occurs along the border regions of Mozambique, Zimbabwe, and Botswana. Some provinces (such as Limpopo, Mpumalanga, and KwaZulu-Natal) are endemic for malaria, posing a risk to approximately 4.9 million individuals, which is equivalent to 10% of the population.[6–8] Malaria transmission follows a seasonal pattern, with cases increasing in October, reaching a peak in January and February, and gradually declining towards May.[6] The majority of South Africans, including those living in regions with seasonal exposure, lack immunity to malaria, placing them at increased risk of developing severe malaria.[7]

Life cycle and aetiology of malaria

Malaria is caused by the protozoan parasite *Plasmodium,* which is transmitted to humans through the bite of an infected female *Anopheles* mosquito. When these mosquitoes feed, they inject sporozoites, the motile and infectious form of the parasite, that initiate malarial infection.[1,9–11] Sporozoites infect the liver cells first, and they undergo an asymptomatic replication cycle lasting seven days.[12] Merozoites are formed and eventually released from the liver cells, subsequently infecting red blood cells (RBCs). During this stage, daughter merozoites undergo a cycle of growth, replication, release, and invasion, while other blood-stage parasites differentiate into male and female gametocytes. This erythrocytic phase leads to symptomatic disease, such as anaemia and splenomegaly, which is mediated by extensive haemolysis.[1,12,13]

For the infection to spread, the female *Anopheles* mosquito must ingest male and female gametocytes. These gametocytes undergo sexual reproduction and maturation inside the mosquito. Mature sporozoites migrate to the salivary gland of the mosquito, where they may infect humans upon their next meal and continue the cycle.[1,13]

In South Africa, the infectious protozoans include *Plasmodium vivax, P. ovale, P. malariae, P. knowlesi,* and *P. falciparum*, with *P. falciparum* being responsible for 95% of malaria cases.[2,3,11]

Incubation period

The interval between being bitten by an infected mosquito and the onset of clinical symptoms varies depending on the *Plasmodium* species causing the infection. In *P. falciparum*, it is usually 10 to 14 days, ranging from as little as seven days to as long as 30 days.[13–15] *P. malariae* can persist at low levels for extended periods, potentially lasting for years. *P. vivax* and *P. ovale* can form dormant stages in the liver (hypnozoites) that persist for months or years after the initial infection. These hypnozoites can eventually reactivate to cause a relapse of symptomatic malaria.[9,10,13]

Symptom manifestation might also be delayed due to incomplete chemoprophylaxis or in patients with partial immunity.[13]

Pathogenesis

The pathogenesis of *Plasmodium* infection can be categorised into three categories: inflammation, anaemia, and end-organ damage.[13]

Inflammation

Inflammation is triggered by parasite metabolism, RBC rupture, and sequestration of infected cells.[13] Hemozoin (a toxic by-product) is produced when heme from haemoglobin is digested by the parasite. Subsequently, macrophages and monocytes release inflammatory cytokines after ingesting hemozoin. This triggers a systemic inflammatory response syndrome, oedema, and increased adhesion of infected cells into small vessels.[13]

Anaemia

Malaria infection induces **anaemia** by causing haemolysis through the replication of parasites, splenic clearance of less flexible RBCs, and the inflammatory suppression of compensatory RBC production. In *P. falciparum* infection, infected RBCs additionally adhere to the blood vessel walls in the spleen, causing a more severe clinical presentation.[13]

End-organ damage

End-organ damage occurs due to cytoadherence of infected RBCs (sequestration) in small blood vessels. Infected RBCs express proteins that cause adhesion to vessel walls and other cells. This cytoadherence, along with clumping of uninfected cells and inflammatory cells, obstructs microcirculation and injures endothelium, causing inflammation and tissue damage. Sequestration can occur in any organ, and, moreover, it prevents parasites from undergoing splenic clearance, thus causing persistent infection.[13]

Box 1: Common malaria symptoms & signs[7,8,14]

Common malaria symptoms & signs include:

- Fever, chills, perspiration, rigours (cold/ hot sweats)
- Headache
- Muscle/joint pain
- Malaise
- Lethargy, fatigue
- Loss of appetite (older children & adults), poor feeding (young children)
- Gastrointestinal symptoms (abdominal pain, diarrhoea, nausea, and vomiting)
- Cough (young children)

Clinical presentation and diagnosis

Malaria symptoms are typically non-specific; thus, the range of potential diagnoses is broad.[2,13,14] No set of signs or symptoms reliably distinguishes malaria from other causes of fever.[2,7] Relying solely on clinical features for diagnosis often leads to overtreatment.[2]

Clinical presentation depends on the causative species.[1] For example, *P. falciparum* is more prone to cause severe infection compared to the other species.[2,3,16–19] However, *P. vivax* can also sometimes cause severe infection due to its ability to cause repeated infections, leading to chronic anaemia.[13]

Uncomplicated malaria

Children often initially present with flu-like symptoms and/ or gastrointestinal symptoms (Box 1). [1,7,9,10,13,19] They frequently develop hepatosplenomegaly and severe anaemia but are less likely to have major organ dysfunction compared to adults.[9,10,19]

Since disease progression can rapidly occur in non-immune patients, high-risk patients (such as children) should be monitored for the first 24 hours of treatment.[7]

Table I: Clinical and laboratory manifestations of severe malaria in children[2,7,9,13,14,18,20]

Signs and symptoms	Definition
Altered consciousness	Blantyre coma score < 3 or altered mental state ranging from irritability, lethargy to coma, stiff neck or bulging fontanelle
Prostration	Generalised weakness causing inability to sit, stand or walk without assistance
Multiple convulsions/seizures	More than 2 episodes in 24 hours
Acidosis	A base deficit > 8 mEq/L or plasma bicarbonate level < 15 mmol/L or venous plasma lactate ≥ 5 mmol/L. Physical manifestations may include respiratory distress (rapid, deep, laboured breaths).
Hypoglycaemia	Blood or plasma glucose < 2.2 mmol/L
Severe anaemia	Haemoglobin level ≤ 5g/dL or haematocrit ≤ 15% in children under 12 years of age
Severe thrombocytopenia	Platelets < 50 x10^9/L
Renal dysfunction	High serum creatinine level for patient's age
Jaundice	Plasma or serum bilirubin > 50 µmol/L or visible yellowing of skin, eyes, etc.
Pulmonary oedema	Radiographic findings and high respiratory rate for patient's age
Significant bleeding	Bleeding from multiple sites such as nose, gums, drip-site, as well as blood in stool, vomit or in urine.
Shock	**Compensated shock:** capillary refill ≥ 3 seconds or temperature gradient on leg, but no hypotension. **Decompensated shock:** systolic blood pressure < 70 mmHg in children, with evidence of impaired perfusion, such as cool extremities or prolonged capillary refill time.
Hyper-parasitaemia	Plasmodium falciparum parasitaemia > 4% or > 3+

Complicated/ severe malaria

Mortality rates in patients who suffer from severe malaria (especially cerebral malaria) approaches 100% if untreated.[3] The severity of malaria infection depends on the level of acquired immunity in children. Immunity develops through ongoing parasite exposure. In endemic areas, children acquire immunity early in life while in non-endemic areas with seasonal transmission, immunity develops incompletely at a later age, resulting in more severe infections in both children and adults.[9] Table I illustrates the clinical and laboratory manifestations of severe malaria in children.

These clinical manifestations may occur together or alone.[13]

Cerebral malaria (CM)

Cerebral malaria (CM) is one of the most concerning clinical complications of malaria, usually attributed to *P. falciparum* parasitaemia.[12,16,18] CM is defined as otherwise unexplained coma or altered mental status (Table I) and/or with seizures in patients infected with malaria.[13,16,18]

Although the exact pathogenesis of CM is controversial, it has been observed that in *P. falciparum* malaria, sequestration of parasites in the small blood vessels of the brain appears to be common. As a result, complications such as cerebral oedema and death occur.[12,13,16,17]

Retinal whitening, vessel discolouring, and white-centred haemorrhages are frequently reported in children with CM and occurs in approximately two-thirds of cases.[16,17,21] CM may cause neurocognitive impairment in 25% of children that last at least two years after exposure. Retrospective trials indicate that these neurologic sequelae may last up to eight years and can include behavioural issues, mental health concerns and the onset of epilepsy.[21]

Diagnostic investigations

Rapid diagnostic tests (RDTs) to detect malaria are available in South Africa, and usually produce a result within 20 minutes.[7,20] A histidine-rich-protein II (HRP2)-based RDT is preferred to detect *P. falciparum*, as > 90% of malaria infections in South Africa are due to this organism.[1,7,13,20,22]

RDTs are highly sensitive, although false negative results are also possible.[9] Reasons such as low parasitaemia, symptom manifestations before parasite multiplication (common in non-immune infants or young children), improper storage or expiry of tests, the prozone effect (saturation of test binding receptors) or parasite genetic variability can cause this phenomenon.[7,9] However, it should be noted that patients can also have positive results up to 30 days after recovery, thus RDTs should not be used for follow-up monitoring.[7,9,20]

Microscopic visualisation of blood smears to identify parasites is the mainstay of diagnosing malaria.[1,9,19] Both thin and thick smears are recommended to confirm malaria diagnosis.[7,9,13,19] If initial RDT or blood smears return a negative result, despite the patient exhibiting symptoms consistent with malaria, and no other cause is identified, tests should be repeated every 6–12 hours until a definitive diagnosis is established.[7] Blood tests for parasites should be conducted regardless of the time of year or whether the patient has taken chemoprophylaxis or travelled to a malaria endemic area.[7]

Polymerase chain reaction (PCR) tests are highly sensitive and specific, however not recommended for routine use due to unpracticality. However, it is useful for identification of species, mixed-infections, and low-level infections.[7,19]

All malaria cases should be reported promptly, as malaria is a notifiable medical condition in South Africa.[7,23]

Prevention strategies

A variety of factors contribute to the risk of travellers acquiring malaria, including patient characteristics, travel activities and the geographic destination.[15,24] A risk assessment is recommended 4–6 weeks before departure, along with education about the consequences of malaria and the importance of preventative measures.[15,24]

Box 2: The "ABC" of malaria prevention:[8,10]

A: **A**wareness and **A**ssessment of malaria risk
B: Avoidance of mosquito **B**ites
C: **C**ompliance with **C**hemoprophylaxis (when indicated)
D: Early **D**etection of malaria disease
E: **E**ffective treatment

Adapted from the South African National Guidelines for Prevention of Malaria

Avoiding mosquito bites

Personal protective measures to avoid mosquito bites should form part of all travellers' prevention strategy, as chemoprophylaxis is not 100% effective.[8,25] Several steps can be taken to prevent mosquito bites, such as remaining inside between dusk and dawn when possible, wearing long, loose, light-coloured clothing, and topical insect repellants.[8]

Topical repellents range from synthetic chemicals to plant-derived products.[15,25,26] The most common are diethyltoluamide (DEET), picaridin, p-menthane-3,8-diol (PMD) and a range of botanical products (e.g. melaleuca, eucalyptus, citronella oils).[25,26] The American Academy of Paediatrics (AAP) recommends topical repellents containing DEET with a concentration of 10–30%.[8,26,27] DEET-containing topical repellents can be applied to uncovered skin during outdoor activities but should not be used on infants under two months old.[8,27,28]

Topical repellents should be reapplied every 4–6 hours, or according to manufacturer instructions. Alternatives such as citronella oils are less potent and shorter acting compared to DEET products.[8,25]

Insecticide-treated nets (ITNs) are an effective and often underutilised prevention measure that is safe for children and pregnant women.[15,25,26,29] Patients should be educated on the effective use of ITNs, such as making sure there are no holes or trapped mosquitos in the net, and that the nets are placed over the bed with edges tucked in.[8,9,15,30] Common insecticides used include permethrin or deltamethrin.[2,10]

Chemoprophylaxis

Antimalarial chemoprophylaxis works by eliminating certain *Plasmodium* parasite life stages in the human host, including liver schizonts, blood schizonts, or dormant hypnozoites.[24]

Table II: Summary of recommended malaria chemoprophylaxis for children:[8–10,15,24,25]

	Mefloquine	Doxycycline	Atovaquone-proguanil
Trade names	Lariam® tabs, Mefliam® tabs	Doxycycline Biotech ®, Cyclidox® caps, Doxycyl® caps	Malanil® tabs, NuMal®, tabs, Malateq®, Mozitec® tabs
Dosing interval	Weekly	Daily	Daily
Paediatric dose	1 tablet = 250 mg mefloquine **Weight: Dose** 5–20 kg: ¼ tablet 21–30 kg: ½ tablet 31–45 kg: ¾ tablet > 45 kg: Adult dose (1 tablet)	2 mg/kg of body weight daily (max 100 mg daily). Children > 15 or > 45 kg should use adult dose of 100 mg daily.	1 paediatric tablet = 62.5 mg atovaquone/25 mg proguanil **Weight: Dose** 11–20 kg: 1 paediatric tablet 21–30 kg: 2 paediatric tablets 31–40 kg: 3 paediatric tablets > 40 kg: 1 adult tablet (250 mg atovaquone/100 mg proguanil)
When to start	Start 1–2 weeks before entering area.	Start 1–2 days before entering area.	Start 1–2 days before entering area.
Duration	Use for 4 weeks after leaving area.	Use for 4 weeks after leaving area.	Use for 7 days after leaving area.
Side effects	Neuropsychiatric side effects: seizures, psychosis, vivid dreams, insomnia. **Other:** gastrointestinal upset, and headaches. Persistent dizziness is rare.	Gastrointestinal side effects, pill esophagitis, photosensitivity, and candida overgrowth.	Typically well tolerated. Gastrointestinal side effects, headaches and transaminitis.
Prophylactic efficacy	Effective against *P. falciparum* but resistance has emerged in parts of Southeast Asia. Effective against *P. vivax*. Limited data on other species.	Effective against chloroquine resistant *P. falciparum*. Limited protection against *P. vivax*.	Effective against chloroquine resistant *P. falciparum*. Effective against *P. vivax, P. ovale* and *P. malariae*.
Special precautions	May cause dizziness and lack of fine co-ordination. Do not use if going for underwater diving, etc.	Use with high SPF sunscreen due to photosensitivity. Patients should avoid milk and dairy products for at least 1 hour before and 2 hours after taking doxycycline. Supplements or antacids containing calcium, bismuth, aluminium, and magnesium should be taken at least 4–6 hours before taking doxycycline.	Take with food/milk for improved absorption. More expensive compared to other regimens, but longer half-life is more forgiving for missed doses.
Population considerations			
Young children	Use only if > 3 months old and > 5 kg. Typically, well tolerated in paediatrics.	Use only in children > 8 years due to risk of permanent teeth discolouration and inhibiting bone growth.	Use only in children > 11 kg.
Epilepsy	Contraindicated. May interact with valproic acid.	May interact with anticonvulsants, possibly resulting in ineffective prophylaxis of malaria.	Can be used.
Long-term use	May be used up to three years.	May be used up to two years.	May be used up to one year.
Diabetics	Insufficient data, use with caution and monitor blood glucose levels.	May cause hypoglycaemia with insulin, monitor blood glucose levels.	No known problems.
Cardiotoxicity or concomitant cardiac medications	May cause conduction abnormalities. Use with caution in patients on beta-blockers, calcium antagonists and quinidine.	Safe to use.	Safe to use.
Renal impairment	Caution (lack of data).	Safe to use.	Contraindicated in creatinine clearance < 30 ml/min.
Hepatic impairment	Contraindicated in severe impairment	Use with caution.	Safe to use in moderate hepatic impairment, but no data on severe impairment.
Psychiatric conditions	Contraindicated, even if only history of depression.	Can be used.	Can be used.

Adapted from South African National Guidelines for Prevention of Malaria and other resources. Refer to National guidelines for safety in pregnancy.

Table III: Dosage of artemether-lumefantrine according to weight bands:[2,7]

Artemether-lumefantrine (Coartem®) 20/120 mg tablets (oral)		
Weight band	**Dosage**	**Total amount for course**
5 to < 15 kg	One tablet immediately, then one tablet after eight hours, then one tablet twice daily for two days	Six tablets
15 to < 25 kg	Two tablets immediately, then two tablets after eight hours, then two tablets twice daily for two days.	12 tablets
25 to < 35 kg	Three tablets immediately, then three tablets after eight hours, then three twice daily for two days.	18 tablets
35 to < 65 kg	Four tablets immediately, then four tablets after eight hours, then four twice daily for two days.	24 tablets
> 65 kg	As for 35 kg, however close monitoring for inadequate response recommended.	24 tablets
> 85 kg	Off-label recommendation is to extend treatment course to five days, administering four tablets per dose for a total of 10 doses.	

Special precautions:
Tablets should be administered with food/milk containing a minimum of 1.2 g fat (e.g. ~100 ml of milk) to ensure adequate absorption.
*The WHO states that it can be safely used in children < 5 kg, but with close observation, however clindamycin + quinine is an effective alternative.[14]
Tablets may be crushed and mixed with a small amount of water (5–10 ml) for immediate consumption for patients unable to swallow tablets whole.

The choice of chemoprophylaxis should be based on patient characteristics, in addition to non-pharmacological prevention strategies.[8] In South Africa, three chemoprophylaxis medications are available, which include atovaquone-proguanil, doxycycline, and mefloquine.[8,24]

It is important to educate travellers that children can still acquire infection while on prophylaxis due to issues such as having trouble taking medications properly, inconsistent adherence and resistance.[9,13]

Medications such as chloroquine and primaquine are no longer recommended due to widespread medication resistance.[2,8,10]

Management of missed doses

If a patient misses a weekly dose of chemoprophylaxis, they should be instructed to take it as soon as they remember and then continue to take it on the normal scheduled day of the week. If more than two days are missed of a weekly regimen, serum levels may be subtherapeutic. However, the patient should still take the dose as soon as possible, with the next dose seven days later and then continue with the weekly regimen thereafter.[24]

Timing is important in daily dosing chemoprophylaxis; thus, doses should be taken at the same time every day. If a dose is missed by 1–2 days, serum levels are unlikely to remain therapeutic. Missed doses should be taken as soon as it is remembered, and the patient should continue with subsequent doses at the same time every day.[24]

Management strategies

The primary goals of malaria treatment include eradicating the parasitic infection, halting its transmission, reducing morbidity, and preventing progression to severe malaria and death. Public health goals include controlling the rise and spread of medication resistance.[2,7]

Uncomplicated malaria

Monotherapy is not recommended for treatment of malaria and contribute to medication resistance.[10]

Artemisinin-based combination therapies (ACTs), such as artemether-lumefantrine (Coartem®), are recommended by the WHO to treat uncomplicated malaria.[2,7] ACTs provide quick clinical response, increased cure rates, decreased malaria transmission and is less susceptible to medication resistance.[2,7] Artemether-lumefantrine boasts with advantages such as short treatment course (six doses over three days) and it is well tolerated.[2,7,31] However, it is only indicated for uncomplicated malaria, as there is no data on its effectiveness in severe disease.[7]

Medication interactions with Coartem®

Lumefantrine levels may decrease in young children (< 3 years), pregnant women, large adults and patients taking mefloquine, rifampicin or efavirenz and in smokers. Closer monitoring of these populations is recommended.[2] Manufacturing recommendations suggest avoiding concomitant use with drugs that prolong the QT interval or are metabolised by CYP2D6 and have cardiac effects.[7]

Alternative treatment options

For children < 5 kg with uncomplicated malaria, the preferred treatment is quinine plus clindamycin, as artemether-lumefantrine use in this population is considered off-label.[7]

Box 3: Dosing of quinine and clindamycin for uncomplicated malaria:

Quinine dose (oral): 10 mg salt/kg body weight every eight hours for seven to ten days.
Clindamycin (oral): 10 mg/kg twice a day for one week.

Quinine syrup is unavailable in South Africa, thus, administering it to children can pose a challenge. One alternative is to crush tablets and mix them with mashed bananas, chocolate syrup, or jam to enhance palatability, although the impact of food on bioavailability has not been investigated.[7]

Children who are unable to tolerate oral medications or have severe vomiting should be given intravenous (IV) artesunate or quinine.[2,7] In cases of *P. vivax* or *P. ovale* infection, primaquine should be given for two weeks to prevent relapse caused by their dormant liver stages.[13,14] To avoid haemolytic anaemia, screening for G6PD-deficiency should be performed.[13,14]

Table IV: Artesunate dosage and administration:[7,14]	
Artesunate (IV)	
Weight	**Dosage**
< 20 kg	3 mg/kg at 0, 12, and 24 hours then daily until able to tolerate oral treatment.
> 20 kg	2.4 mg/kg at 0, 12 and 24 hours, then daily until able to tolerate oral treatment.
Administration	
Dissolve 60 mg artesunate powder in 1 ml 5% sodium bicarbonate solution (supplied with the artesunate powder). Add 5 ml 5% dextrose (or 0.9% sodium chloride) to give a solution of 10 mg/ml for injecting as a **bolus into an IV cannula**. Once reconstituted, artesunate solution is not stable and should be administered within 30 minutes; solution not administered within 30 minutes should be discarded.	

Severe malaria

Severe infection warrants prompt parental treatment as death can occur within hours of presentation.[13]

Artesunate

Globally, IV artesunate is strongly recommended as evidence shows improved mortality rates compared to quinine.[7,10]

Artesunate is safe and is tolerated well. Common adverse effects such as gastrointestinal upset and dizziness have been reported. Rare side effects include blood dyscrasias (neutropenia, decreased reticulocyte counts, anaemia, and eosinophilia), elevated aspartate transaminase (AST), and transient electrocardiogram (ECG) abnormalities.[7] Cases of haemolytic anaemia, occurring more than one week after treatment with artesunate, have been documented in African children with high parasite counts and non-immune European travellers.[2,7] Due to this phenomenon, patients with high parasitaemia should be monitored closely to detect late-onset anaemia.[2,7]

Quinine

Quinine is recommended if artesunate is not available.[7]

Quinine should always be administered **via slow, rate controlled IV infusion** and never through bolus. A loading dose should be given, followed by maintenance dose eight hours after starting the loading dose. After which, maintenance therapy should be given every eight hours until the patient can use oral treatment.[7] Absorption in obese patients may be erratic, and ideal body weight should be used to calculate doses.[7]

General measures

General measures in managing severe malaria in young children include assessing and stabilising airway, breathing, and circulation (ABC). Hypoglycaemia, cerebral malaria, anaemia, and metabolic acidosis are important complications and should be monitored for. Agitation and respiratory distress due to metabolic acidosis signal poor prognosis. Fluid replacement via crystalloids is recommended, while boluses should be avoided. Children have an increased risk for dehydration. Third generation cephalosporins should be administered to children with severe malaria as secondary bacterial infections or sepsis are common. Seizures may be subtle in children, and underlying causes could be hypoglycaemia, CM, or fever.[2,7,9,14]

Box 2: Quinine dosage:[7]
Quinine loading dose: 20 mg/kg quinine dihydrochloride salt, diluted in 5–10 ml/kg 5% dextrose and given IVI over four hours.
Quinine maintenance dose: 10 mg/kg quinine dihydrochloride salt, diluted in 5–10 ml/kg 5% dextrose and given IVI over two to four hours.

Note: Do not confuse doses of salt and base. Doses are usually prescribed as salt (10 mg salt = 8.3 mg base).[7]

Future directions

Recently, vaccination has become a part of the armamentarium used to prevent malaria.[2,16] The RTS,S/AS01 malaria vaccine is recommended by the WHO for the prevention of *P. falciparum* malaria in children living in moderate to high-risk endemic areas.[2,3,32] However, it is currently not yet available in South Africa.

In a large phase three randomised controlled trial in over 15 000 children in SSA, the vaccine was deemed efficacious, however several safety concerns emerged. Severe adverse events and deaths occurred at similar rates in control and intervention groups. Febrile seizures were slightly more common in the 2–3 days after the RTS,S/AS01-vaccinated children but not infants. Meningitis and CM occurred more frequently among vaccinated girls compared to control groups. While these findings may have been attributed to chance given the large sample size of the study, their severity warrants further investigation in real-life pilot programmes to establish risk-benefit ratios.[32]

In contrast, a recent qualitative study found that caregivers had positive perceptions about the malaria vaccine for children, with fewer admissions to hospital and cost benefits. Healthcare workers played a crucial role in vaccine uptake. Fear of unknown side effects were identified as possible barriers to recommending the vaccine to other caregivers.[33]

A second vaccine, R21/Matrix-M (R21), is recommended by WHO since October 2023 for children living in high-risk areas.[3]

Conclusion

Worldwide efforts against malaria have recently hit a standstill, and continued interventions are needed to get countries back on track.[3] South Africa has shifted from malaria control towards malaria elimination, however majority of cases in the country is

now imported, and often present late to facilities in malaria-free regions.[7,23]

Healthcare professionals in South Africa, regardless of whether they work in malaria-endemic regions, should be knowledgeable about malaria prevention and treatment for travellers.[7,8,24]

Educating travellers to malaria-endemic countries about preventative steps is the best way to encourage adherence and preventing transmission. If malaria infection does occur, a high index of suspicion, rapid diagnosis and urgent treatment is vital to prevent severe illness and death, especially in children.[7,10,16]

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Emerging paradigms in prebiotics research: implications for human health and nutrition

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Abstract

Introduction: Understanding the complex link between our gut health and general well-being has drawn more attention in recent years. Prebiotics can promote mineral absorption, influence metabolism, improve immune system regulation, and fight infections.

Aim: This article focuses into the evolving paradigms in prebiotics research, highlighting their regulation, diverse applications, impact on diseases, and their growth on the global market.

Discussion: Prebiotics are Generally Recognized as Safe (GRAS), novel foods and food additives by the Food and Drug Administration (FDA), EU and Japan, respectively. The multifaceted applications of prebiotics go across various sectors, ranging from functional foods and dietary supplements to cosmetics. A comprehensive review of prebiotics' effects on human health and illness prevention is a significant strength of the paper. Prebiotics support a healthy microbiome by feeding helpful gut flora, which may reduce the risk of a variety of illnesses and improve general health. In parallel, it covers an overview of the prebiotics industry in the world, considering aspects including consumer knowledge of gut health and growing prebiotic demand.

Conclusion: Prebiotics are anticipated to have a significant role in determining the direction of nutrition and preventive healthcare as research advances and consumer demand for natural health solutions rises.

Keywords: prebiotics, diseases, applications, regulation, United States of America, European Union, Japan

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Introduction

The field of prebiotics research has witnessed a significant evolution in recent years, driven by advancements in understanding the intricate relationship between gut microbiota and human health. The idea of prebiotics has drawn a lot of interest and is the category of compounds that the gut flora breaks down.[1] The gut microbiota refers to the diverse group of microorganisms that live inside the human gastrointestinal system.[2] According to the report, the human colon contains 10^{10} to 10^{12} live microorganisms per gram.[3] The stomach, small intestine, and large intestines are resident for multiple microbial colonies known as gut microbiota, which are essential for maintaining human health, where mostly anaerobes reside in the large intestine.[4] *Lactobacilli* and *Bifidobacteria* should be the kind of bacteria that are activated.[5]

A prebiotic is defined as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improves host health", according to Gibson and Roberfroid.[6] They presented the idea of prebiotics as an alternate strategy for modifying the gut flora. Over the past 15 years, prebiotics have been the topic of much investigation in an effort to comprehend their mechanisms of action and clarify the positive health benefits they have on the human host.[5]

There are a few criteria to follow for an ingredient in food to qualify as a prebiotic, such as,

- Not being absorbed, resisting gastric acidity or hydrolysed in the upper digestive tract;
- It is fermented by intestinal microflora
- function as a selective substrate for one or a small number of helpful bacteria that are naturally present in the colon and are encouraged to develop and/or become metabolically active.
- Instigate systemic and luminal impacts that are advantageous to the host's health.[7]

Consequently, they have the power to change the colony's flora in favour of a healthier composition. Various polysaccharides, oligosaccharides, microalgae, and uncultivated plants from a variety of sources are typically referred to as prebiotics.[8] The main sources of newly discovered prebiotics include algae, fruit juice, seeds and peels, traditional Chinese medicine, and other microorganisms that contain polymers, polyphenols, and polypeptide polymers.[9,10] Prebiotics must be able to endure digestive processes before they reach the colon in order to have these effects, and they should ideally remain throughout the large intestine so that the advantages can be seen, such as the ability to improve immune system control, resist infections, affect metabolism, boost mineral absorption, and improve health.[11]

The creation of completely novel candidate prebiotic substances has been made possible by the objective of promoting a larger variety of microbial species.[4] Candidate prebiotics include certain peptides, proteins, and lipids (both ethers and esters) that cannot be digested, such as certain oligo and polysaccharides.[12] These substances cannot be digested by human digestive enzymes or absorbed in the upper gastrointestinal system due to their

Table I: Important prebiotic and their potential benefits[15]

Prebiotic types	Chemical Ccontent	Methods of production	Potential benefits
Fructooligosaccharides (FOS)	Two-to-one glycosidic connections connect the units of glucose and fructose.	Monomers of fructose are polymerised.	Boost immunity, lower triglycerides, enhance mineral absorption, suppress pathogenic germs, prevent cancer, and manage diabetes
Galactooligosaccharides (GOS)	Glucose and galactose are linked together via β (1→3) and β (1→4) connections.	Lactose transgalactosylation with -galactosidase	Boost bifidogenic activity
Xylooligosaccharides (XOS)	Xylose units linked through β (1→4) bonds	Plant xylans are hydrolysed by enzymes.	Non-oncogenic nature, demonstrate a favourable impact on the flora in the intestinal tract, and are not digestible
Soybean oligosaccharides (SOS)	Terminal galactose (Stachyose) connected to (Raffinose)galactose -(1–6)	Not Specified	Boost IgG levels, control the weight of the body, and strengthen immune response
Isomaltooligosaccharides (IMO)	Up to eight glucose monomers formed by α (1→6) glycosidic linkage	Liquified starch transglucosylation, extraction from honey, fermentable foods	Boost the gut flora
Fructans	Fructose with β (2→1) linkage	Hydrolysis by enzymatic means utilising fructozyme L	Alter gut physiology to offer protection from infections and raise glucose levels
Guar gum	D-mannopyranosyl (1–4) and D-galactopyranosyl (1–6) residues joined together	Utilising cellulase for enzymatic hydrolysis	Increase blood sugar and cholesterol
Pectin oligosaccharides (POS)	(1–4)-α-D-GalA (galacturonic acid) -(1,2)-α-L-Rha	Pectinase's enzymatic degradation of water	Anti-inflammatory effect
ß-glucans	Glucose molecules linked together by beta-glycosidic bonds	Pleurotus sp. (pleuran) mushrooms, extraction from natural sources followed by purification processes and from yeast	Gut health promotion, immune support, antioxidant activity, cholesterol management, and blood sugar regulation
Inulin-type fructans	Fructose molecules linked together by β(2→1) bonds, with a terminal glucose molecule	Roots of traditional Chinese medicine *Morinda officinalis* or Indian mulberry	Composition and activities of the gut microflora, stool production, absorption of Ca and other minerals, production of gastrointestinal endocrine peptides, immunity and resistance to infections, Lipid homeostasis

chemical structure.[13] These substances, which are often called "colonic foods," are foods that transit through the gastrointestinal system and serve as substrates for endogenous colonic bacteria, giving the host energy, metabolic substrates, and essential micronutrients.[14]

There are many types of prebiotics where largely consist of oligosaccharide carbohydrates (OSCs), which are a subset of carbohydrate families (further explained in Table I).

Prebiotics can improve the healthy gut microbiota, which has a positive impact on host health, significantly affecting the gut flora and leading to favourable impacts on metabolic function.[16] They are transformed in the intestinal tract by bacteria from the gut because host enzymes are unable to break them down.[17] According to Alomaim, altering lipid metabolism can improve calcium absorption, which benefits bowel and immune system functions.[17,18] The effects of prebiotics have been studied in a

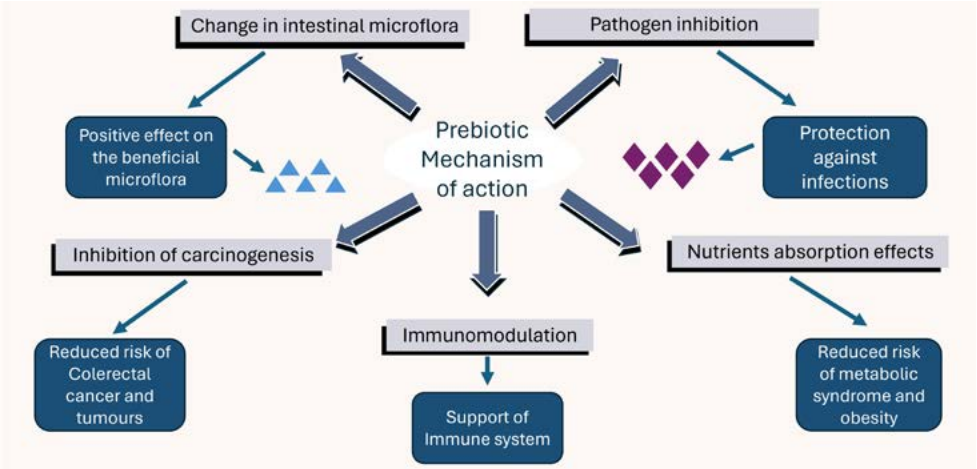

Figure 1: Combined overview of the metabolic efficiency and immunomodulation effects of prebiotics

number of fish-based trials. When selected prebiotics (β-glucan, galactooligosaccharides, and maltooligosaccharides) were administered to *Channa* striata fingerlings, improvements in growth performance, nutrient digestibility, immune regulatory gene expression were observed when compared to probiotics.[19] Based on their structure and composition, certain bacteria can utilise them as a source of carbon and energy.[4] There have been a number of models put up that can demonstrate the prebiotic effect in various bodily regions.[20] The metabolic efficiency and immunomodulation effects of prebiotics represented in Figure 1.[21] The article covers the impact of prebiotics on various diseases, its regulatory requirements, applications on different areas and the global market scenario.

Regulations

Regulation is considered for prebiotics, as well as for many other types of food and dietary supplements, to ensure their safety, efficacy, and proper labelling.[22] The regulation of prebiotics is essential to safeguard public health, enhance consumer confidence, and ensure that prebiotics deliver their intended health benefits without causing harm.[23] Consumers should look for prebiotic products that comply with relevant regulations and are backed by scientific evidence to make informed choices about their health and well-being. Regulation helps determine the positive effects and health benefits of prebiotics by assessing scientific evidence and clinical studies to support claims related to their impact on gut health, immune function, and overall well-being. It also ensures that prebiotics are safe for consumption and do not pose any risks to human health (such as assessing potential allergenicity, toxicity, and any adverse effects associated with their use). The Consumer Protection Act ensures that consumers are not misled by false or exaggerated claims about the benefits of prebiotics.[24] These health claims made on product labels or in advertising must be authorised and supported by scientific evidence. To fulfil the requirement mentioned above, regulations must be followed as per the regulatory bodies.[25]

Prebiotics are not specifically governed by a single worldwide regulatory organisation, but depending on the region, they might be covered by a number of different regulatory bodies.[26]

United States of America (USA)

Prebiotics are categorised as dietary ingredients, which are items that are meant to be ingested as part of a diet. Vitamins, minerals, herbs, botanicals, and other substances are all included in the category of dietary ingredients, which are regulated by the Food and Drug Administration (FDA) agency as per the regulatory framework. The definition of dietary ingredients includes some prebiotic compounds such as fibre, oligosaccharides, and indigestible carbs.[27] The FDA controls them in accordance with its regulatory framework. Prebiotics are regarded as dietary supplements when they are advertised and sold as stand-alone goods in the form of pills, capsules, tablets, or powders.[28] The Dietary Supplement Health and Education Act (DSHEA) of 1994 mandates that the FDA regulate dietary supplements.[29] Dietary supplement producers are required to guarantee product safety, accurate labelling, and adherence to good manufacturing practices (GMPs). The FDA manages the voluntary Generally Recognised as Safe (GRAS) notification system, which enables producers to confirm the security of fresh or existing substances, including prebiotics.[30] When a substance is deemed GRAS, it signifies that qualified professionals generally concur that it is secure when used as intended. Manufacturers are able to submit a GRAS notification to the FDA, supplying data and scientific proof to back up the safety conclusion. Although the GRAS designation is not required for prebiotic compounds, it gives businesses a way to verify safety.[31] The FDA controls prebiotic product labels to ensure accuracy and ward off false advertising. Prebiotic product health claims must adhere according to the Federal Food, Drug, and Cosmetic Act's regulations. Prebiotics may make qualified health claims that are backed by scientific evidence but do not fulfil the criteria for an authorised health claim that requires a large amount of scientific agreement. Qualified health claims are those that describe the structure or function of the prebiotic and how it helps preserve normal body processes. The FDA is in charge of ensuring that prebiotic labelling and health claims adhere to these rules.[32] In the United States of America (USA), a variety of federal and state laws, rules, and organisations are in charge of regulating consumer protection. The main federal body tasked with upholding consumer protection rules is the Federal Trade Commission (FTC) Act in 1914.

European Union (EU)

The European Food Safety Authority (EFSA) analyses health rights regarding food items inside the European Union (EU). According to EU regulation 2015/2283, prebiotic compounds may be approved as novel foods.[26] They need approval before they can be sold in the EU. The European Commission must receive a dossier from the manufacturers outlining the prebiotic's benefits and safety. The dossier should provide thorough details about the prebiotic's composition, manufacturing process, suggested applications, and intended intake levels.[33] The safety assessment should also include scientific data, such as possible allergenicity, toxicological, and dietary factors.[34]

Some of the prebiotic health claims, such as those for chicory inulin, have been authorised. Before 1997, inulin, GOS, and FOS were utilised in the EU and are regarded as safe food components. Prebiotic medications created after 1997, however, are seen to be distinct and require safety approval; certain Human milk oligosaccharides (HMOs) for example, are given this designation.[35] To present, the EU has only issued one prebiotic, chicory inulin, a health claim saying that it "improves bowel performance". This approval based on data demonstrating that there is a causal connection between ingesting a non-fractionated mixture of monosaccharides (10% of total carbohydrate), disaccharides that contain inulin-type fructans, and inulin obtained from chicory with a mean degree of polymerisation (DP) of 9, and the maintenance of normal defecation as demonstrated by an

increase in stool frequency.[36] This approval is based on data demonstrating that there is a causal connection between ingesting a non-fractionated mixture of monosaccharides (10% of total carbohydrate), disaccharides that contain inulin-type fructans, and inulin obtained from chicory with a mean DP of 9. This connection is associated with the maintenance of normal defecation, as demonstrated by an increase in stool frequency.[36] For the evaluation, the European Commission sends the file to the EFSA for review. Based on the provided information, the EFSA evaluates the prebiotic substance's safety and any claimed positive effects. The European Commission considers the assessment after the EFSA evaluation and decides whether to approve the prebiotic ingredient as a new food. The prebiotic may be sold and used in the EU market if approved. Considering the labelling specifications, a prebiotic substance must adhere to the EU's labelling criteria once it has been approved as a new food. The prebiotic's features and the circumstances under which it should be used should be accurately represented on the label. It should not deceive customers and should give them the information they require about the product.[37]

Japan

Prebiotics are categorised in Japan as Specified Functional Ingredients (SFI). They are compounds with functional qualities and health advantages that have been scientifically proven.[38] This group includes prebiotics, which encourages the development and activity of beneficial microorganisms in the stomach.[39]

The approval process in Japan requires manufacturers to submit safety and efficacy data to the Ministry of Health, Labor and Welfare (MHLW) for permission before using prebiotics in food and health products. The information should back up the claimed functional qualities or health advantages as well as show that the prebiotic is safe. This may consist of research investigations, clinical tests, or other pertinent scientific data.[40] The MHLW examines the manufacturer's effectiveness and safety data. To ascertain if the prebiotic satisfies the requirements for approval, they evaluate the scientific data. Prebiotics must pass this review procedure to be used in foods and healthcare items.[22] In Japan, any claims about the health benefits of food and health products containing prebiotics must be backed up by data from credible sources. In order to confirm the veracity of the alleged health advantages, the MHLW assesses the documentation offered by the producers to ensure that customers are given accurate and trustworthy information about the goods they use. For pharmaceutical products, prebiotics may also be utilised as components in medicinal goods and food items. The Pharmaceuticals and Medical Devices Agency (PMDA) issued laws and guidelines for the approval and use of pharmaceutical substances must be followed in certain situations by manufacturers.[41]

South Africa

The South African Health Products Regulatory Authority (SAHPRA) of South Africa (SA) would generally regulate prebiotics. The term "novel fibres" in South Africa refers to "edible carbohydrates," which have been found to have a physiological impact that is beneficial to health and have been approved and registered by the SAHPRA.[42] This has been confirmed by widely recognised scientific evidence. Novel fibres are defined as any oligomers (FOS), polymers (inulin), or mixtures thereof whose DP varies from 2 to 60 monomeric units for which a prebiotic claim could be made. They can also be defined as having $10 monomeric units, not hydrolysed by the endogenous enzymes in the human small intestine, produced synthetically, or derived from natural sources that are not typically consumed as fruits, vegetables, or cereals in the diet. The following criteria should be used to demonstrate prebiotic activity: the ability to withstand gastric acidity, the breakdown of food by mammalian enzymes and GI absorption; fermentation by intestinal microbiota; the induction of bifidobacteria growth throughout the entire indigenous population; and the specific induction of growth and/or activity of other indigenous GI microbiota that contribute to health and well-being.[43]

How does the regulations in USA, EU and Japan impact on SA regulations?

When establishing its own prebiotic regulatory framework, SA looked to the laws of the USA, EU, and Japan as significant models. The FDA, EFSA, and MHLW have created standards, safety procedures, and documentation criteria that SA can use to guarantee the efficacy, safety, and calibre of prebiotic products sold in its market. By matching SA's standards with internationally accepted norms, harmonising legislation with these top countries helps improve international commerce and foster consumer trust. SA can create strong evaluation procedures, precise labelling regulations, and efficient consumer protection measures by utilising the knowledge and best practices of these nations. This will improve public health outcomes and create an atmosphere that is favourable for the expansion of the prebiotic industry.[44]

Impact of prebiotics on diseases

The gut microbiota, an intricate ecology made up of trillions of bacteria, is found in the human gut.[45] The vital function that these gut microorganisms play in preserving general health and avoiding numerous illnesses has been highlighted by recent studies mentioned in the sub-sections below.[46]

Irritable bowel syndrome (IBS) and Crohn's disease

Irritable Bowel Syndrome (IBS) is a digestive illness categorised by persistent stomach discomfort and irregular bowel movements without any apparent biological reason. In one case study, 44 IBS patients participated in a randomised, double-blind, cross-over experiment.[46] The treatments include placebo followed by low-dose GOS (3.5 g/d) over a four-week period, placebo followed by high-dose GOS (7.0 g/d), and placebo followed by placebo. Lower ratings for gas, bloating, and overall alleviation were achieved in the low dosage prebiotic group compared to placebo due to more *Bifidobacteria* in these groups than in the placebo group.[46]

Crohn's disease, which affects the whole digestive system, including the mouth and the anus, is a chronic, recurrent ailment.[47,48] There is compelling evidence that the GI microbiota is closely related to the genesis of the disorder, making prebiotics an interesting therapy option for Crohn's disease. Studies have revealed that people with Crohn's disease had lower relative levels of *Bifidobacteria*.[49] The pathophysiology of Crohn's disease may be linked to this decline in *Bifidobacteria* population, which may contribute to dysbiosis and inflammation in the gut.[50]

In a group study from 2011, people with Crohn's disease benefited from taking 15 g/day of FOS for four weeks because it boosted the *Bifidobacteria* population in their stools.[51] However, the other double-blind, randomised, and placebo-controlled studies failed to show any therapeutic advantages for giving patients who are suffering with active Crohn's disease 15 g/day of FOS.[52]

Acute gastroenteritis

Everyone will likely experience acute gastroenteritis at some point. Typically, it entails consuming food or water that has been tainted with pathogenic bacteria or their poisons. Examples of typical causative agents include *Shigella*, *Yersinia enterocolitica*, *Salmonellae*, *Campylobacter jejuni*, strains of *E. coli*, cholera-causing bacteria *Vibrio cholera*, and *Clostridium perfringens*. Pathogens can either emit toxins that contaminate food before it is consumed, or they can colonise and proliferate in the gastrointestinal system before invading host tissue.[53] Such toxins impair the intestinal mucosa's ability to function, resulting in nausea, vomiting, and diarrhoea. One or more potential mechanisms at work include competitive effects from occupation of common immigration sites, lead antagonism by way of natural antimicrobial excretion, and competition for vitamins. The gut pH of a microniche may be lowered by the metabolic byproducts of these bacteria, such as acids secreted, to levels below which pathogens may successfully compete.[53] One of the studies published in the journal, includes 200 children aged 1-5 years, divided into four groups with 50 children where each received prebiotics in different manner with particular dose.[54] All patients' hospital stays, the number of diarrhoeal and vomiting episodes they experienced before and after treatment, the amount of intravenous fluid therapy they received before and after treatment, and any additional complications that occurred over the course of the trial were compared. An effective study outcome revealed that the group receiving prebiotic and bovine colostrum outperformed other groups across various metrics, including the length of hospital stays, the frequency of vomiting and diarrhoea bouts, the severity of electrolyte disturbance, the technique of rehydration, and any associated consequences. There was no apparent distinction in the groups' pretreatment clinical state.[55]

Colorectal cancer

The third most prevalent type of cancer globally is colorectal cancer, which progresses in phases beginning with a genetic mutation, adenomatous polyps, and ultimately aggressive and metastatic malignancy.[56] By inducing apoptosis, prebiotic fermentation products like butyrate have been demonstrated to both lower the incidence of colorectal cancer and decrease its progression. Additionally, a clinical study showed that symbiotic therapy (*Bifidobacterium lactis* and *Lactobacillus rhamnosus* combined with inulin) could decrease the impacts of colorectal cancer by decreasing colorectal cell growth and causing necrosis in colonic cells, which enhances the strength and efficiency of the epithelial barrier.[57]

Necrotising enterocolitis

A disorder known as necrotising enterocolitis (NEC) causes parts of the colon to swell and become necrotic and most common in preterm newborns.[58] High rates of morbidity and mortality may result from it. Prebiotics like FOS and GOS are thought to prevent NEC because they increase the proliferation of gut microbiota (like *Bifidobacteria*) and decrease the number of harmful bacteria in preterm newborns. Additionally, SCFAs can increase eating tolerance by promoting intestinal and stomach motility. The concentration of faecal *Bifidobacteria* might be increased by FOS, GOS, or their combination, according to a meta-analysis of four randomised controlled trials, however, the risk of developing NEC and its development were not significantly impacted.[59] Therefore, further clinical studies must be conducted to clarify the precise of prebiotics on NEC.[60]

Psoriasis

Chronic inflammation leads to unchecked keratinocyte proliferation and improper differentiation, which is the root cause of psoriasis, an autoimmune pathogenic chronic inflammatory skin disease.[61] Prebiotics have the potential to alter the gut flora and enhance gut health include inulin and oligosaccharides.[61] They can reestablish the equilibrium of the gut's microbes and encourage the development of advantageous bacteria. Prebiotics have been shown in certain instances to treat psoriasis through altering the gut microbiome. Faeces from 30 people with psoriasis and 30 healthy controls were included in the study. Bioinformatic methods like Phylogenetic Investigation of Communities by Reconstruction of Unobserved Taxa and Quantitative Insights into Microbial Ecology (QIIME) were used to assess the makeup of the gut microbes. The findings indicated that patients with psoriasis had higher virtual abundances of specific bacterial taxonomy, such as faecal bacterium and *Megamonas*, compared to healthy people.[62] Numerous cytokines are implicated in the pathogenesis of psoriasis as primary impact molecules. Interleukin-2 receptor in particular exhibited a favourable link with *Phascolarctobacterium* and a negative interaction with the *Dialister* in terms of inflammation-related parameters. *Phascolarctobacterium* and *Dialister* relative abundances is used to predict the severity of psoriasis. According to the association study using markers of inflammation and microbiota, microbiota dysbiosis may cause an aberrant immune response in psoriasis.[63]

Cardiovascular disease

Cardiovascular disease (CVD) incidence has risen to the point that it is now the chief cause of death globally in recent decades.[64] A

connection between diet and cardiovascular events has been demonstrated through the elements of metabolic syndrome and obesity, including dyslipidaemia and the presence of visceral fat. It is well-recognised that oxidative stress contributes to the development of CVD. This condition is associated with increased intracellular oxygen radical levels that harm DNA, proteins, and lipids. Inulin and oligofructose, two prebiotic dietary supplements, aid in reducing oxidative stress.[65] Inulin has the ability to scavenge reactive oxygen species (ROS) thanks to short-chain fatty acids. Inulin can also prevent the gut from becoming inflamed and regulate how the body responds to pathogenic bacterial assaults (LPS). This is probably because it activates the body's defences against ROS by upregulating colonic mucosal detoxifying enzymes (GSTs), which in turn aids in restoring the levels of several crucial proteins involved in the contraction of intestinal smooth muscle.[66]

High cholesterol and blood pressure

In a hypercholesterolemic rat model, prebiotic treatment reduces total serum cholesterol, according to Parnell and Reiner.[46] Prebiotics also lower cholesterol levels. In this study, rats were fed one of three diets that included 0, 10, or 20% prebiotic fibre for ten weeks. In both doses, prebiotic fibre reduced blood cholesterol levels by over 25%. This change was accompanied by an increase in caeca digesta and the increased expression of bile and cholesterol-producing genes. Additionally, the liver triacylglycerol buildup in the obese rats receiving a 10% prebiotic supplement was reduced by almost 40% (Table I). Obesity and the development of CVDs are frequently linked, but several clinical studies have revealed that probiotic and prebiotic supplementation have anti-obesogenic properties.[67]

Diabetes mellitus (DM)

There is proof that the solubility of fibre lowers postprandial insulin and serum glucose levels by raising the consistency of nutrients in the small intestine, delaying the release of glucose, preventing glucose from binding to the fibre and lowering the amount of available fibre for use, and inhibiting the action of amylase on amido.[68] Due to their ability to form gels, inulin and FOS have an impact on how well nutrients, particularly carbohydrates, are absorbed by delaying gastric emptying and/or shortening intestinal transit time. Yacon ingestion can regulate blood sugar, however, the exact mechanism by which this happens is yet unclear. Prebiotic supplement treatment was found to be associated with an increase in plasma gut peptide concentrations (peptide YY and glucagon-like peptide 1), which may explain changes in hunger and satiety.[69] Recent *in vitro* research has shown that a specific concentration of long-chain water-extractable arabinoxylans (LC-AX) stimulates specific intestinal microorganisms, like *Bifidobacterium longum*, and starts specific fermentation patterns that may be advantageous to the host (like the production of propionate). Human investigations have shown that long-term administration of LC-AX can aid type II diabetics in regaining their ability to respond to glucose and insulin.[70]

Osteoporosis

Increasing calcium and magnesium absorption can help prevent diseases like osteoporosis and is essential for bone formation. Rats' ability to absorb calcium and magnesium can be improved by adding GOS to their diets.[71] Although the authors noted that there are likely both microbial and non-microbial mediated processes, the precise mechanism in this instance is unknown, therefore, a colonic flora is necessary for GOS to have this impact.[72] In experiments on humans, 15 g of oligofructose or 40 g of inulin per day appeared to improve the apparent absorption of calcium (FOS can also alter mineral absorption). It has also been demonstrated that consuming FOS causes an increase in magnesium absorption.[73]

Lipid regulation

The control of lipids may be affected by prebiotics as well. A study on diabetic rats found that when XOS (Xylooligosaccharides) was used as a substitute for simple carbohydrates in the meals, liver triglyceride increased to a level comparable to that of healthy rats, lowering the blood cholesterol and triglyceride elevations connected to diabetes.[74] Studies have shown that prebiotics may have cholesterol-lowering effects in both animals and humans.[75]

Prebiotics, such as fructans, have been found to exhibit interesting serum or hepatic lipid-lowering properties. Additional research on FOS has shown that it also reduces blood lipids.[76] Prebiotics can help treat hyperlipidaemia caused by diabetes and other illnesses, but they haven't been shown to lower lipid levels in healthy people.[75,77]

Alzheimer's disease

Amyloid and malfunctioning tau protein buildup in the brain, together with the eventual onset of dementia, are hallmarks of Alzheimer's disease.[78] Key factors in the progress of Alzheimer's disease and the deposition of amyloid are acute and chronic neuroinflammation. Pro/prebiotics, such as lactic acid bacteria and *Bifidobacterium*, have drawn interest in this context as methods for reducing neuroinflammation.[79] The probiotic "*Bifidobacterium breve* strain A1" taken orally prevented the cognitive deterioration seen in rats with Alzheimer's disease. *Bifidobacterium breve* A1 ingestion reduced amyloid-induced immune-reactive genes and inflammation in the hippocampus, according to gene profiling study.[80]

Female reproduction

Since birth until adolescence, *Lactobacilli* species have predominated in the vaginal microenvironment.[81] After puberty, cleanliness, hormonal changes, menstruation, illnesses, and sexual activity all affect the variety of microorganisms. Because of this variability in the vaginal environment, *Lactobacilli* species are not commonly found in most women, and subsequently, there's a higher vulnerability to urogenital illnesses, including bacterial vaginosis and urinary tract infections. Bacterial vaginosis (BV) has been linked to a higher risk of preterm birth and a lower likelihood

of getting pregnant. Prebiotics may help with fertility, according to certain animal studies.[82] Prebiotics, for instance, have been linked to better embryo implantation and higher ovulation rates in animal models.[16]

Human health benefit

Any intervention, including the use of prebiotics, should have, as its major goal enhancing health and, as a result, lowering the risk or severity of sickness. Health end points targeted in human trials of orally administered prebiotics are discussed in Table II. The best strategies focus on prevention and acknowledge that early interventions that support a resilient, diverse, and healthy microbiome have the greatest potential to improve health overall.[83]

Table II: Health end points targeted in human trials of orally administered prebiotics[22]

Health end point	Prebiotic used
Diabetes type 2, the metabolic disorder, high cholesterol levels, and arthritis are all associated with being overweight or obese.	Inulin, GOS, FOS
Stimulation of gut bacteria that produce neurochemicals	GOS
Improved calcium and other mineral absorption, bone health	FOS, Insulin
Enhanced water retention, reduced erythema, and improved skin health	GOS
Allergy	GOS, FOS
Inflammatory bowel disease	Lactulose, inulin,
Urogenital health	GOS
Infants' intestine habits and overall gut health	FOS, GOS,
Vaccine response and infections	FOS, GOS, polydextrose
In preterm newborns, necrotising enterocolitis	GOS, FOS
Irritable Bowel Syndrome	GOS
Traveller's diarrhoea	GOS

Applications of prebiotics

In food

Prebiotics must not have a detrimental effect on the product's organoleptic properties in order to be used in food products. Additionally, it must maintain its stability while being used to prepare food, which entails high temperatures, low pH, or a combination of the two, as well as conditions that encourage Maillard reactions.[84] Prebiotics can be manufactured as a powder, syrup, or capsules and sold as supplements at health food shops or included in food items. Prebiotic powder can be placed on foods or mixed into drinks, or capsules can be taken with meals.[85] Applications and properties of prebiotics is mentioned in the Table III.

Prebiotics are used as functional ingredients in the food industry for beverages, wellness drinks, spreads, dairy products (powdered milk, cheese, fermented milk, ice cream, fruit juices, tea, coffee, chocolate, soft drinks in general, isotonic drinks, liquid sugar, and alcoholic beverages are among these drinks), infant food, and weaning foods. Along with meat products, dry quick meals, canned food, and sweets (jellies, puddings), candies, chocolates, chewing gum, cakes, biscuits, morning cereals, breads, and pastas, other uses include soups, sauces, and dressings.[86]

Table III: Application and functional properties of prebiotics[87]

Application	Functional Properties
Dairy products	Fibre and prebiotics, fat or sugar substitution, texture and tongue feel
Frozen desserts	Substitution of fat or sugar, texture, and melting behaviour
Fruit Preparations	Synergy of sugar substitute sweeteners, body and mouth sensation, and fibre
Beverages and drinks	Tongue sensation, foam stability, replacement of fat or sugar, and prebiotics.
Baked goods and breads	Sugar substitution, retention of moisture, fibre, and prebiotics
Breakfast cereals and extruded snacks	Sugar substitution, sharpness and expansion, fibre and prebiotics
Filling	Replacement of fat or sugar, texture, and tongue sensation
Dietetic products	Fibre and prebiotics, as well as fat or sugar substitution
Sugar confectionary	Sugar substitute, resistance to heat, and fibre
Chocolate	Fibre, a sugar substitute, and heat resistance
Soups and sauces	Prebiotics and sugar substitution
Meat Products	Fibre, fat substitution, and textural constancy

Infant formulas that include prebiotics

Infant formula is an alternative to human milk if the mother is unable to breastfeed. In order to provide nutrition equal to that of mother's milk, infant formulas must have ingredients that mimic HMO (Human milk oligosaccharides). Using a combination of short-chain GOS and long-chain FOS in place of HMO allows for gut microbial stimulation on par with that found in the mother's milk.[88] By transgalactosylating lactose, B-galactosidases operate as a catalyst and exhibit prebiotic action in the synthesis of GOS.[89] Depending on their structural composition, GOS and other oligosaccharides generated from lactose have important biological activities. For instance, by adhering to glycan-binding proteins of pathogens or to glycan-binding domains of bacterial adhesins and toxins, they might modify immune responses.[90] Sucrose is employed as a substrate for the generation of FOS utilising a mixed enzyme system that includes glucose oxidase and b-fructofuranosidase. Commercial baby formulae were examined for prebiotic oligosaccharides utilising chromatographic techniques including HPLC-RID and GC-FID. The results were in line with the GOS, FOS and GOS/FOS ranges that were specified on the labels of these packaged formulations These ranges were 1.6-5.0, 1.7-3.2, and 0.08-0.25/2.3-3.8 g/100 g product, respectively.[91]

In cosmetic industry

Skin care solutions that are made with prebiotic components like xylitol, rhamnose, glucomannan, oligosaccharides, inulin and others assist to maintain the skin's surface healthy, prevent symptoms of aging, enhance general skin health, etc.[92]

Other components high in prebiotics that are used in skin care products include oats, which help to soothe irritated skin; ginseng, which lessens skin inflammation; and pine, which shields the skin from UV rays, as discussed in Figure 2.[93]

1. Prevents breakouts of acne

Prebiotics are an effective treatment for some forms of acne outbreaks, including cystic acne as it combats any skin irritation that can cause an outbreak.[94] Research found that the prebiotic element glucomannan, when paired with probiotic compounds, successfully treats acne.[94] Prebiotics and probiotics work together to increase the effectiveness of probiotics' ability to keep acne-causing bacteria away from the skin.

2. Calms skin

Prebiotics made from sugar have calming qualities that aid to soothe inflamed skin.[4,95] Prebiotic serums are often mild and beneficial for sensitive skin which has reputation for lowering skin sensitivity. Prebiotics will help in case the user experiences rashes, inflammation, or redness.

3. Other advantages

- Preserves the pH balance of the skin; decreases blemishes[96]
- Encourages youthful skin[93]
- Control aging symptoms[97]

Global market scenario of prebiotics

Over the coming years, market growth is anticipated to be aided by rising demand for supplements and rising consumer knowledge of fibre's health benefits. The industry is also anticipated to grow as prebiotic natural herbs are grown and harvested more often throughout Europe.[99] The prominent players that are operating in the global prebiotics market in which some of them are Bright Food (Group) Corp. Ltd., Abbott Laboratories, BENEO GmbH, Cargill Inc., Kraft Foods Group, Inc., Cosucra Groupe Warcoing SA, The Kraft Heinz Company, Friesland Campina, Jarrow Formulas, Inc., Parmalat S.p.A, Royal Coson, Roquette Frères, Yakult Honsha Co., Ltd.[100]

The corporations are ramping up their new product development, mergers & acquisitions, and strategic expansion efforts. For instance, "BENEO" stated in March 2020 that it will invest more than EUR 50 million in a significant expansion of its chicory root manufacturing facility in Chile by the year 2022.[101]

There is no indication of an upgrade for BENEO's chicory root processing facility in Chile in 2024. Nonetheless, it is claimed that BENEO, with an investment of more than EUR 50 million, announced a major expansion for its chicory root production facility in Chile by 2022. After completion, the extension at Pemuco, Chile, allowed for the processing of its liquid chicory root fibres. The expansion was a component of BENEO's broader investment plan, which also included the completion of a second refining line in Pemuco, Chile, and capacity augmentation measures at practically every location.[102]

Prebiotics can be used for a variety of other purposes, including enhancing food texture and naturally sweetening it. Fructo-oligosaccharide (FOS) and inulin, two crucial prebiotic components, are in great mandate in the products which requires a calorie-free sweetening flavour.[86] Through the foreseeable term, this is boosting the overall growth of the prebiotics business. Prebiotics are even utilised more often in animal feed since they improve the general well-being such as enhancing the health, absorption, and productivity and metabolism of the animals, which have anticipated to contribute to the spectacular global market boom. Other factors influencing the market's growth include the increasing reliance on animals as a source of protein and the expanding usage of prebiotics in chicken feed to boost productivity.[103]

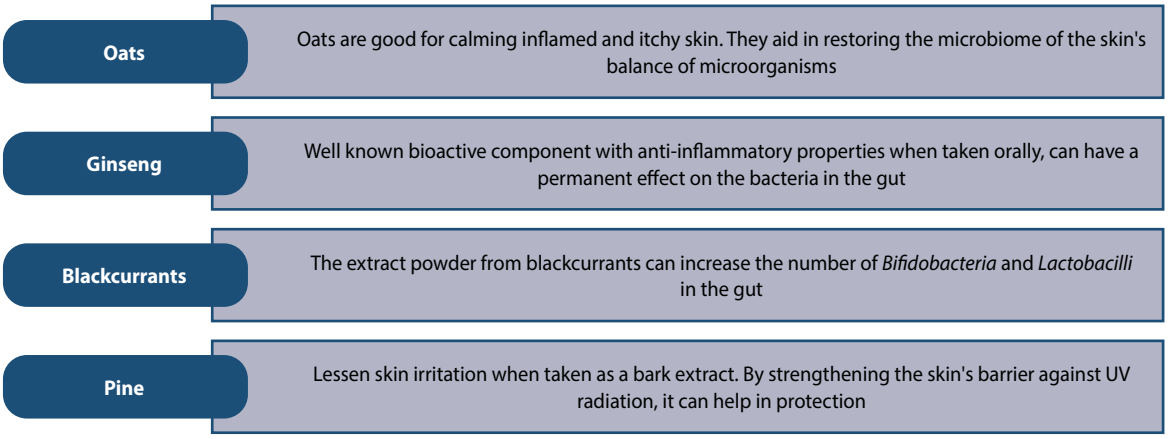

Figure 2: Application of prebiotics in cosmetics[91,93]

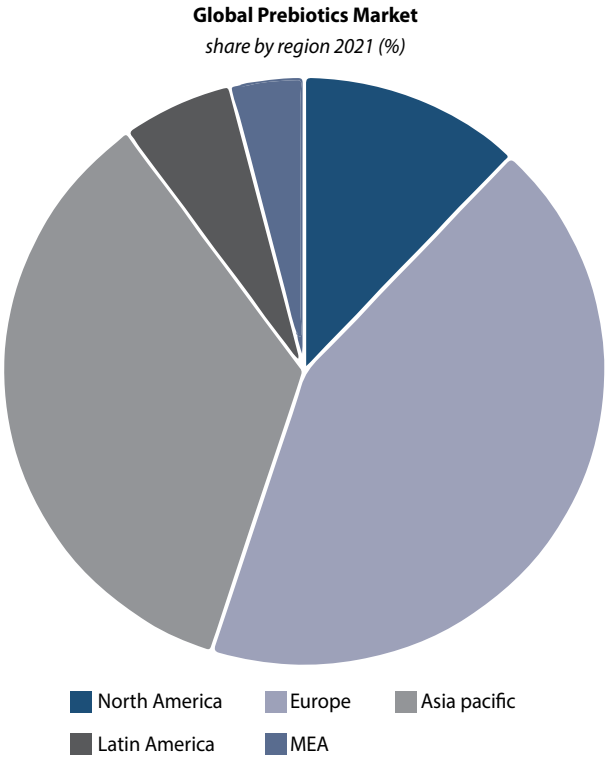

Figure 4: Projected market growth rates (2022-2030) with Asia Pacific leading at 15.4% CAGR, driven by product diversity. Europe dominated in 2021, while North America's growth remains constant.[106]

Prebiotics market in the world by region

The regions of the Asia-Pacific region, USA the EU, South America and the Middle East and Africa (MEA), make up the worldwide prebiotics market.[104] The prebiotics market is dominated by the Asia-Pacific region. The Asia Pacific market is expanding due to demand from countries with large populations and high dairy product consumption, such as India, Japan and China. Throughout the forecasted period, higher grade components for animal feed are now required due to the growing significance of animal feed components, which will be tracked by the high prevalence of illnesses like Porcine Epidemic Diarrhoea Virus (PEDv) and Bovine Spongiform Encephalopathy (BSE) (Figure 4).[105]

Prebiotics market worldwide by application

Prebiotic foods, drinks, and nutritional supplements such as dairy products, baked goods, cereals, dry food prebiotics and fermented meat products used in animal feed make up the three application-based segments of the worldwide prebiotics market.[107] Prebiotic dietary supplements are further divided into infant formula, specialist nutrients, food supplements, and nutritional supplements. The prebiotics business has been dominated by the prebiotic food and beverage market and are projected to be used more often in the food and beverage sector because of the presence of colon bacteria that promote good health as depicted in Figure 5.

Demand for these products is expected to rise as consumers become more aware of how protein may promote appropriate nutritional levels and preserve muscle strength. Additionally, it is believed that leading a healthy and active lifestyle and being more aware of the advantages of protein can significantly contribute to promoting the use of dietary supplement products.[108]

Inulin, Mannan-oligosaccharides (MOS), Galacto-oligosaccharides (GOS), and others (Oligosaccharides, chicory fructans, which is HMO, and XOS) have also been classified as subgroups of the worldwide market. In 2021, the inulin ingredients market sector held a commanding market share of more than 37% of the total revenue.[109] The rising demand for inulin in baked goods and drinks is likely to have a substantial impact on the segment's growth throughout the forecasted period. The demand for GOS products worldwide is anticipated to increase significantly between 2022 and 2030, based on the market trends and analysis.[110]

Conclusion

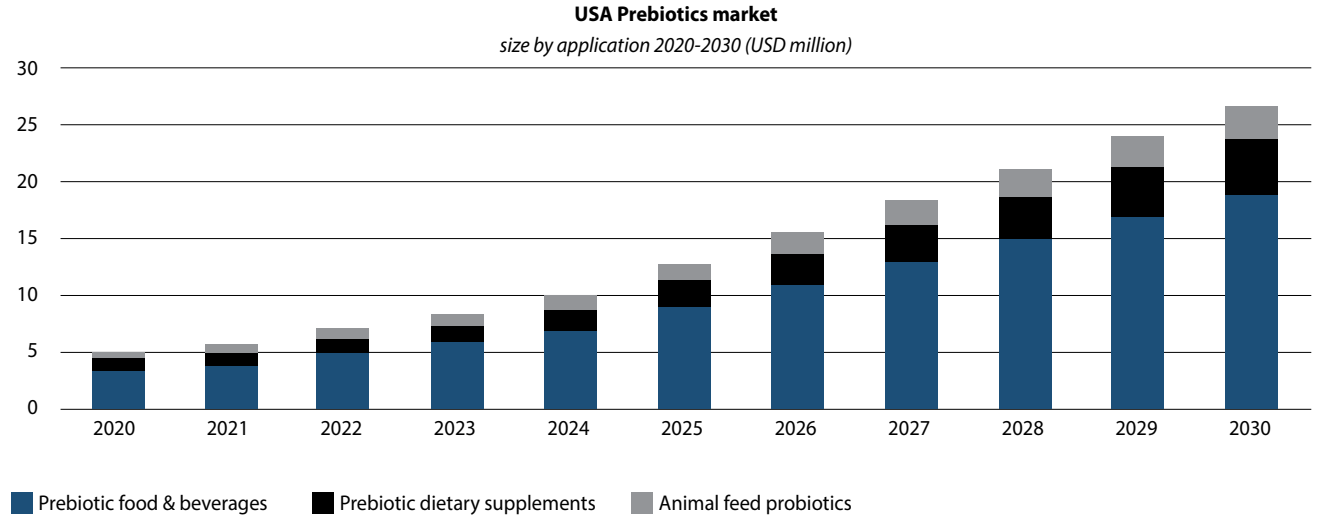

Figure 5: USA Prebiotics Market by Application (2020-2030, USD million). In 2021, the application category for food and beverages held a dominant market share of over 82.00% of the worldwide volume. Due to the expanding significance of animal proteins and the fortification of animal feed with bacteria that enhance animal gut health, the demand for prebiotics in animal feed was high globally in 2021 and is expected to rise even higher.[109]

Prebiotics are widely used as dietary food ingredients since they support healthy gut flora and may be obtained naturally from a variety of meals. Their inclusion in the food can increase health of the human and shield against a variety of diseases. Prebiotics must be regulated in order to guarantee their efficacy, safety, and appropriate labelling. The applications of prebiotics span a wide range of industries, from functional foods and dietary supplements to pharmaceuticals and animal feed. Prebiotics have been shown to be beneficial in the prevention or treatment of necrotising enterocolitis, acute infectious diarrhoea, acute respiratory tract infections, diarrhoea linked to antibiotic use, and colic in infants. Leveraging scientific advancements, adhering to regulatory standards, and staying responsive to consumer preferences is crucial for unlocking the full potential of prebiotics in shaping a healthier world. By capitalising on these insights, businesses, policymakers, researchers, and investors can contribute to the growth of the prebiotics market and foster innovative solutions for improved gut health and overall wellness. Looking to the future, personalised nutrition, novel prebiotic sources, synbiotic formulations, and exploring the gut-brain axis are poised to shape the prebiotics industry.

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Update on the pharmacological management of neurodegenerative diseases: Alzheimer's disease

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Abstract

Neurodegenerative diseases (NDDs) are the most common causes of morbidity and cognitive impairment, particularly among the elderly population worldwide. Due to increasing life expectancy, there has been an increase in the prevalence of NDDs. One of the most common NDDs is Alzheimer's disease (AD), which is characterised by a complex, multifactorial irreversible aetiology, including the progressive loss of neurons. It is also the most common cause of dementia. Pathologically, AD is associated with the presence of amyloid plaques and intracellular neurofibrillary tangles. The management of AD focuses mainly on establishing an early, accurate clinical diagnosis, early drug administration, treatment of comorbidities and dementia-related complications, as well as treatment of behavioural and psychological symptoms. There is currently no cure for AD, and the currently United States Food and Drug Administration (US-FDA) approved drugs only offer symptomatic relief aiming to improve cognitive and behavioural symptoms; however, they do not target the underlying AD pathology or prevent neuronal degeneration. The current US-FDA approved drugs used for the management of AD include acetylcholinesterase inhibitors (donepezil, galantamine, and rivastigmine), N-methyl-D-aspartate (NMDA) receptor antagonist (memantine), and monoclonal antibody against Aβ (Lecanemab). It should be noted that all these approved drugs only assist in the management of symptoms; however, they do not prevent neuronal loss, brain atrophy, and progressive deterioration of cognition associated with AD. To curb the increasing prevalence of AD, new therapeutic strategies are required, including the development of gene therapy, drugs targeting Aβ, and drugs targeting neuronal hyperexcitability among others.

Keywords: alzheimer's disease, cholinesterase inhibitors, dementia, lecanemab, memantine, neurodegenerative diseases

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Introduction

Neurodegenerative diseases (NDDs) are characterised by a gradual loss of neurons, resulting in progressive dysfunction of synapses, neurons, glial cells, and their networks.[1,2] NDDs are common causes of morbidity and cognitive impairment worldwide, particularly in the elderly population.[3] This is mainly due to the collapse of the structure and function of neural networks and loss of neurons in several areas of the central nervous system (CNS), resulting in the breakdown of the core communicative circuitry, culminating in impaired memory, cognition, behaviour, sensory, and/or motor function.[4] Thus, NDDs are associated with cognitive, psychiatric, and motor deficits due to atrophy of the affected regions.[5] The clinical manifestation of a particular NDD reflects the region of the brain that is involved and the specific population of cells that are affected.[6] Due to increased life expectancy and changing population demographics, NDDs have become more common, and they account for a significant and increasing proportion of morbidity and mortality.[7] NDDs encompass a broad range of neurological diseases, including, among others, Alzheimer's and Parkinson's diseases. However, the most prevalent form of NDD is Alzheimer's disease (AD). Thus, this review will provide an overview of the diagnosis and management of AD.

Alzheimer's disease

AD is defined as an irreversible and incurable progressive NDD characterised by memory impairment and cognitive decline that can affect behaviour, speech, visuospatial orientation, and motor function.[8,9] AD is pathologically defined by extensive neuronal loss and the accumulation of intracellular neurofibrillary tangles and extracellular amyloid plaques in the brain.[10] It is the most common cause of dementia, which accounts for approximately 50–70% of dementia cases.[11,12] Age is regarded as the main risk factor for AD, as its prevalence tends to increase exponentially with age.[8,12] It has been reported that the risk of AD doubles every five years after the age of 65 years, with those over the age of 85 years having a 50% chance of developing AD.[13] Due to an increase in life expectancy, the prevalence of AD has increased.[14] However, ageing alone may not be sufficient to induce AD. It has been reported that AD affects approximately 10% of people over the age of 65 years and 50% of those over the age of 85 years.[8] However, it has also been occasionally reported in individuals over the age of 20 years, mainly due to genetic predisposition.[8]

Pathologically, AD is characterised by neurodegeneration, neuronal loss, and atrophy, particularly in the temporal and parietal lobes of the brain.[13] However, the key pathological hallmarks of AD are the presence of amyloid plaques and neurofibrillary tangles.[13,15,16] The pathogenesis of AD is complex and multifactorial; however,

the most common factors are amyloid plaques and intracellular neurofibrillary tangles, which contain abnormally phosphorylated tau protein aggregated into filaments.[17,18] The amyloid plaques first develop in brain areas associated with cognition and spread to other cortical areas as the disease progresses.[19] AD has been associated with the accumulation of insoluble forms of amyloid-β (Aβ) plaques extracellular spaces and blood vessel walls and aggregation of the microtubule protein, tau in neurofibrillary tangles in neurons.[20]

The second distinguishing feature of AD is the accumulation of neurofibrillary tangles in neurons, which are mostly formed by chemically altered (abnormally folded and phosphorylated) tau protein.[19] In addition, neuropil threads, dystrophic neurites, associated astrogliosis, microglial activation, and cerebral amyloid angiopathy that frequently coexist, have been reported.[21] These pathological processes may induce neurodegeneration with synaptic and neuronal loss, resulting in macroscopic atrophy.[21] The neuronal loss tends to regularly appear in the neocortex, hippocampus, amygdala, and basal nucleus of Meynert thus, impairing the function of these brain regions.[22] This in turn may result in progression from episodic memory loss to a slow global decline of cognitive function, which characterises AD.[23] In addition, these pathological changes in AD are accompanied by decreased acetylcholine concentrations in the basal forebrain, which results in reduced cognitive function, as well as glutamate excitotoxicity, and ultimately in neuronal apoptosis.[18]

Diagnosis of Alzheimer's disease

Early diagnosis plays a crucial role in the management of AD and may be a determinant of the disease outcome. However, clinical diagnosis has been challenging, especially in the early stages of AD due to symptoms being mistakenly associated with the normal consequences of aging.[8] It has been reported that the earliest and most salient aspect of AD is episodic memory impairment, which reflects an inability to effectively encode and store new information.[24] This memory impairment may be associated with the normal ageing consequences. Thus, it is important to confirm AD diagnosis. The diagnosis of AD is based on a comprehensive assessment that includes a thorough medical history, as well as clinical, neurological, biofluid (cerebrospinal fluid (CSF) and blood) testing, and psychiatric examinations.[8,25] Thus, the diagnostic assessment of patients suspected of having AD comprises the following: i) history (family, medical, neurological, and neuropsychiatric) from a reliable source; ii) physical and neurological examination; iii) routine laboratory examinations (complete blood count, sequential multiple analysis-21, thyroid function test, vitamin B_{12}, folate, and rapid plasma regain); optional laboratory examinations (erythrocyte sedimentation rate, human immunodeficiency virus (HIV) serology, serology for Lyme's disease, urinalysis, urine drug screening, lumbar puncture, and electroencephalography); and iv) neuroimaging (computed tomography (CT) or magnetic resonance imaging (MRI) scan).[8,19]

Currently, only a probable diagnosis of AD can be made clinically, with a definite diagnosis only achievable after postmortem through several neuropathological assessments.[15,26] Clinical diagnosis of AD involves a detailed history of the type and course of symptoms from both the patient and another source (partner or family member) to assess whether there is cognitive impairment and whether social, occupational, or other instrumental functions are affected, and also involves neuropsychological assessments such as orientation, memory, and concentration tests.[15] The commonly used diagnostic criteria for AD were initially outlined by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) joint task force in 1984.[14] These criteria primarily depend on the exclusion of other dementias; however, relative accuracy is low.[25] It is important to note that not all dementias are caused by AD and can be differentiated by their signs and symptoms.[8] Criteria for probable AD include dementia with cognitive deficits in at least two cognitive domains including progressive memory loss, normal level of consciousness, including, onset between ages 40–90 years, and the absence of another plausible medical explanation.[14,27,28]

Criteria for possible AD include all those listed for probable AD; however, these are often accompanied by another illness that might be contributing to the symptoms but not necessarily the primary cause of dementia and progressive focal cognitive deficit.[14,27,28] Therefore, the inclusion of laboratory analyses such as CSF testing is essential to confirm the diagnosis.[29,30] It has been recommended that the diagnosis should incorporate biomarkers associated with the pathophysiological processes of AD.[27,28] Research suggests that the early stages of AD may induce changes in CSF levels of multiple markers, including Aβ and tau proteins,[30] which are the most established AD fluid biomarkers.[28] It has been reported that the biomarkers of brain Aβ protein deposition are low CSF Aβ and positive positron emission tomography (PET) amyloid imaging, and the biomarkers of downstream neuronal degeneration are elevated CSF tau (total and phosphorylated), decreased fluorodeoxyglucose (FDG) uptake on PET in the temporo-parietal cortex, and disproportionate atrophy on structural MRI.[27,28] The diagnosis of definite AD is regarded as the gold standard and requires neuropathological assessments such as an autopsy or brain tissue biopsy, which can only be conducted by a neuropathologist.[14,25] An autopsy is mainly used to confirm clinical assessment and to assess any comorbidities that may have contributed to cognitive impairment.[31]

AD progresses slowly into three clinical stages, i.e. mild, moderate, and severe; however, these often overlap with the normal ageing process.[8] In the mild stage of AD, patients exhibit short-term memory impairment, often accompanied by symptoms of anxiety and depression, and this stage usually lasts for approximately 2–3 years.[32] The moderate stage of AD is mainly characterised by neuropsychiatric manifestations such as hallucinations, delusions, and reversal of sleep patterns, while the severe stage of AD is mainly characterised by motor signs such as motor rigidity and prominent cognitive decline.[32]

Table I: Approved drugs for the treatment of AD

Class	Drug	Indication	Notes
Acetylcholinesterase inhibitors	Donepezil	Mild to moderate AD.[18,35]	Well tolerated but may have GIT effects. May be combined with Memantine.[18,35]
	Galantamine	Mild to moderate AD.[18]	Well tolerated but, may have GIT effects.[35]
	Rivastigmine	Mild to moderate AD.[18,35]	Well tolerated but, may have GIT effects.[35]
N-methyl-D-aspartate receptor antagonist	Memantine	Moderate to severe AD.[18,35]	Use with caution in patients with renal or liver diseases. May be combined with Donepezil.[18,35]
Monoclonal antibody against Aβ	Lecanemab	Early AD (mild cognitive impairment/ dementia).[45-47]	Elevated levels of Aβ plaques should be confirmed before initiating it.[46,47] Monitor amyloid-related imaging abnormalities (ARIA). May also cause headache.[45]

AD, Alzheimer's disease; Aβ, Beta-amyloid; GIT, Gastrointestinal tract; ARIA, Amyloid-related imaging abnormalities

Pharmacological management of Alzheimer's disease

The management of AD focuses mainly on establishing an early, accurate clinical diagnosis, early drug administration, treatment of comorbidities and dementia-related complications, and treatment of behavioural and psychological symptoms.[33] However, the management of AD has long been challenging as its pathogenesis is complex, making it an area of research interest.[34] As previously mentioned, AD is an irreversible and progressive disease. Thus, there is currently no cure. Both non-pharmacological and pharmacological strategies have been employed in the management of AD; however, this review focuses on the pharmacological strategies. The currently approved treatments for AD are only symptomatic in nature with the aim of improving cognitive and behavioural symptoms; however, they do not target the underlying pathology, nor have they been shown to completely protect neurons.[35-39] Most drug development programs target disease modification with agents that prevent or delay the onset or slow down the progression of AD.[36] Thus, the main objectives of AD management are to relieve cognitive, behavioural, and psychological symptoms; and to slow down progression of the disease.[40] There are currently five individual drugs and one drug combination that have been approved by the United States Food and Drug Administration (US-FDA) for the treatment of AD (Table I).[18] For the treatment of mild to moderate AD, the following acetylcholinesterase inhibitors (ChEIs) have been approved, i.e. donepezil, galantamine, and rivastigmine, while memantine (an N-methyl-D-aspartate (NMDA) receptor antagonist) has been approved for the treatment of moderate to severe AD.[18,35,41]

The rationale for the use of ChEIs is based on the cholinergic hypothesis, which states that cognitive dysfunction and other symptoms of AD may be due to the loss of cholinergic neurons.[35] The ChEIs inhibit the acetylcholine esterase enzyme, which breaks down acetylcholine in the synaptic cleft. In so doing, ChEIs prevent acetylcholine hydrolysis, thus increasing its synaptic levels resulting in enhanced cholinergic transmission.[35] All three US-FDA approved ChEIs are well tolerated by patients; however, the most common adverse events have been linked with the gastrointestinal (GIT) effects such as nausea, vomiting, diarrhoea, and anorexia.[35] The efficacy of these ChEIs are comparable, and their selection is merely based on cost, individual patient tolerance, and physician experience.[42] It has been shown that excessive activation of NMDA receptors by glutamate (main excitatory neurotransmitter in the CNS) increases the vulnerability of CNS neurons to neuronal degeneration.[34,43] Excessive activation of NMDA receptors results in the intracellular accumulation of calcium (Ca^{2+}), which initiates a cascade of events resulting in neuronal death.[44] Memantine is a non-competitive, moderate-affinity, phencyclidine-site, NMDA antagonist that protects neurons from glutamate mediated excitotoxicity without preventing the physiological activation thereof.[34,39,44]

Furthermore, monoclonal antibodies that target Aβ are currently under investigation. Aducanumab (Aduhelm) was the first therapy to demonstrate the reduction of cognitive and functional impairment by removing Aβ from the brain.[45] As a result, it received accelerated approval in 2021, however it has since been discontinued by the manufacturer (Biogen).[45] However, this decision was not prompted by concerns regarding safety or efficacy. Fortunately, recent approval by the US-FDA has paved the way for Lecanemab (Leqembi), a recombinant humanised immunoglobulin gamma 1 (IgG1) anti-amyloid monoclonal antibody that binds to amyloid oligomers, protofibrils and insoluble fibrils, and also targets Aβ in the brain.[45,46] Leqembi has been shown to reduce Aβ and improve cognitive function.[45,46] Thus, it is empirical to first confirm elevated levels of Aβ plaques prior to prescribing Leqembi. However, the only drug combination that has been approved by the US-FDA is donepezil and memantine.[18] All these approved drugs only assist in the management of symptoms; however, they do not prevent neuronal loss, brain atrophy, and progressive deterioration of cognition.[35]

Conclusion

NDDs like AD present ongoing challenges globally. Despite a rising prevalence associated with increased life expectancy, advancements in AD management have been limited. Furthermore, the complex and heterogeneous nature of the disease poses significant hurdles in the management thereof. There is currently no cure for AD, and the currently US-FDA approved drugs are only symptomatic in nature with the aim of improving cognitive and behavioural symptoms, they do not target the underlying

AD pathology. The current US-FDA approved drugs used in the management of AD include ChEIs (donepezil, galantamine, and rivastigmine), NMDA receptor antagonist (memantine), and monoclonal antibody against Aβ (Lecanemab). It should be noted that while these drugs only assist in the management of symptoms, they do not prevent neuronal loss, brain atrophy, and progressive deterioration of cognition associated with AD. Agents targeting the underlying pathology of AD are required, including combination therapy. To curb the increasing prevalence of AD, novel therapeutic strategies are required, including the development of gene therapy, drugs targeting Aβ, and drugs targeting neuronal hyperexcitability, among others. Continued improvements in current therapies may lead to the development of effective agents that enhance cognitive function and protect against neuronal loss to address the unmet needs of AD patients.

Conflict of interest

The authors declare no financial or other competing interests that might have influenced the performance or presentation of this work.

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The misuse of analgesics and nonsteroidal anti-inflammatories in runners

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Abstract

Global participation in running has continued to grow over the last decade, with millions of people running weekly, regardless of distance. These events, particularly endurance running events, require months of progressive training and load adjustment, which, combined with other factors, increase the risk of developing running-related injuries. Inflammation is a natural biological response important for healing in musculoskeletal tissue; however, it may also contribute to the unpleasant experience of pain. Runners may suffer from exercise-induced pain and inflammation, necessitating using analgesics and nonsteroidal anti-inflammatories. Unfortunately, the inappropriate use of these drugs is frequently seen in athletes, which may impact their recovery after injury or general health status. This review presents in brief the current knowledge of running-related pathology and treatment thereof, including considerations of its misuse.

Keywords: analgesics, inflammation, nonsteroidal anti-inflammatories, pain, running

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Introduction

Running has grown in popularity over the last decade, with millions of individuals running weekly.[1] This popularity is observed for distances ranging from 5 km to ultra-marathon distances, where long-distance events require a greater degree of training when compared to shorter distances.[1] This increased demand for endurance running events, in combination with other factors, increases the risk of developing running-related injuries (RRI).[1] Athletes may suffer from exercise-induced pain and inflammation,[1-3] which are commonly observed with endurance running due to the nature of the event.[4] Inflammation is important for healing in musculoskeletal tissue; however, it may also contribute to pain, which can be an unpleasant experience.[3] Unfortunately, many athletes do not give themselves sufficient time to recover when injured or overworked, which results in support-seeking measures to get them back on their feet.[5] Pharmacologically, analgesics and anti-inflammatories, such as nonsteroidal anti-inflammatory drugs (NSAIDs), would generally be used to mitigate the effects of RRI and exercise-induced pain and inflammation.[1-3] Such pharmacotherapy is turned to due to their accessibility.[5] There are multiple studies which have assessed the frequency of use of NSAIDs during endurance events.[6-8] Many athletes believe that analgesics and anti-inflammatories improve performance and allow for the prophylactic management of injuries. Therefore, the use and misuse thereof are prevalent in sports, including endurance running.[5] Additionally, between 2009 and 2014, the number of individuals taking part in marathons increased worldwide by 13.25%, with average completion times indicating a high proportion of non-elite runners.[1] This more diverse range of runners includes individuals with comorbidities who may be more at risk of NSAID-associated adverse effects.[1]

Studies suggest that runners have poor knowledge of the correct use and associated side effects of analgesics and anti-inflammatories.[3-4,6] Athletes have been shown to take analgesics prior to a marathon, where such use has been associated with drug-induced side effects (including stomach cramps and gastrointestinal bleeding).[1] Analgesics, such as NSAIDs, may precipitate cardiovascular and gastrointestinal events, with gastric ulcers, myocardial infarctions and strokes being prominent concerns.[9] Moreover, the use of NSAIDs in athletes is believed to be detrimental to muscle healing and has a high risk of exceeding the recommended dosages.[6,9] This paper will review the prevalence of the use of analgesics and NSAIDs in runners and the associated risks in the context of running.

Inflammation and pain

Pain, an extremely complex phenomenon, is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[3] Pain is influenced by culture, previous pain events, mood and the ability to cope with the sensation.[3] There are two main types of pain: nociceptive and neuropathic pain.[10] Nociceptive pain is the result of neuronal activity in response to actual tissue damage or in stimuli that is potentially tissue-damaging.[11] Neuropathic pain is chronic and is characterised by nervous system lesions or dysfunction.[11-12] Neuropathic pain can be maintained by several mechanisms, with one common example being diabetic peripheral neuropathy present in 50% of diabetic patients.[11-12] Given the pathophysiological pathways involved, each type is treated differently from a pharmacotherapeutic vantage.[10] For example, depending on the severity, nociceptive pain will be treated with NSAIDs and opioids, whereas neuropathic pain is treated with antidepressants, anxiolytics or antiepileptic drugs (such as gabapentin).[10]

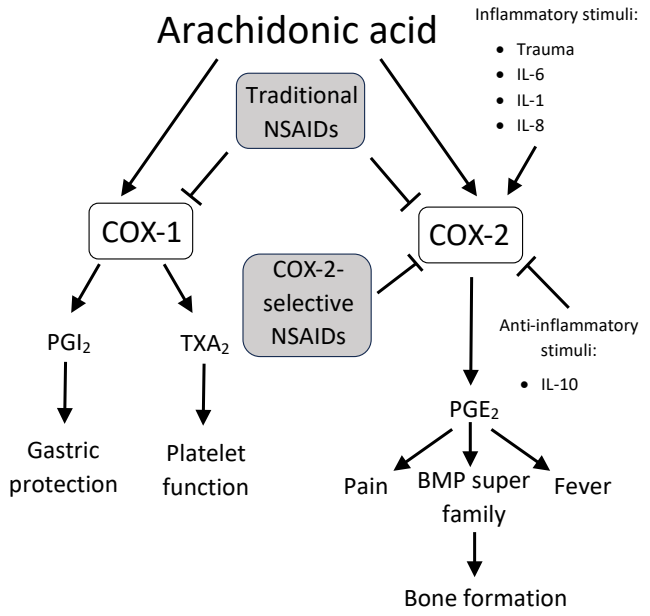

Figure 1: The synthesis of prostanoids and their associated biological effects.[15] TXA_2 = thromboxane A_2. COX-1 = cyclooxygenase-1; COX-2 = cyclooxygenase-2; PGI_2 = prostaglandin I_2; PGE_2 = prostaglandin E_2; IL-6 = interleukin-6; IL-1 = interleukin-1; IL-8 = interleukin-8; IL-10 = interleukin-10; NSAIDs = nonsteroidal anti-inflammatories; BMP = bone morphogenetic protein.

There are two forms of pain: acute pain, which has a limited duration, and chronic pain, which persists beyond the accepted time of healing.[3] When tissue injury occurs, phospholipids are released from the cell membrane and converted to arachidonic acid by the enzyme phospholipase A_2.[13] Arachidonic acid is then converted by the enzyme cyclooxygenase (COX) into various prostanoids, including prostaglandins (PGs).[13] The PGs are responsible for mediating pain and inflammation, e.g. those resulting from sports injuries.[3]

The COX enzyme is available in two isoforms: COX-1 and COX-2 (Figure 1).[13] Both isoforms are found throughout the body.[2] The COX-1 isoform is constitutively expressed and serves a homeostatic role.[2,13] In the gut, PGs, specifically PGE_2, play a role in gastro-protection and maintenance of several key functions of the GI tract.[13] Additionally, the prostanoids thromboxane A_2, PGs (E_1, E_2 and E_3) and prostacyclin play a role in platelet aggregation.[13] The PGE_2 also plays an important role in sodium and water retention in the kidney.[13] The COX-2 isoform is released by pro-inflammatory cytokines, mitogens and endotoxins in inflammatory cells.[13-14] Once stimulated, COX-2 produces the PGs, which are responsible for pain and inflammation.[13] Therefore, inhibition of COX-2 using NSAIDs helps to mitigate the pain and inflammation mediated by the COX-2-produced PGs.[13]

Muscle soreness versus muscle injury in running

Muscle soreness induced by prolonged exercise, as in the case of marathon running, is referred to as early-onset muscle soreness (EOMS).[16] The muscle soreness and damage markers in EOMS are different from those seen in delayed-onset muscle soreness, seen after eccentric muscle contraction, which occurs during resistance training.[16] Running longer distances, such as marathons, places enormous mechanical stress on one's body, which leads to muscle damage.[16] For example, gastrocnemius damage has been reported after a marathon due to the mechanical stress of the distance.[16] Increased creatinine kinase and lactate dehydrogenase plasma concentrations after a marathon are indicators of cellular damage which persist for approximately four days after a marathon, suggesting the muscle soreness will subside after several days.[16] It is apparent that muscle soreness induced by running long distances is a natural physiological response to the mechanical stress placed on the body whilst running.[16]

Running injuries may be defined in several ways,[17] for example, an injury requiring medical attention,[18] by the time needed for an athlete to return to running, or by a feeling of pain or discomfort.[17,19,20] A drawback to running is the relatively high risk of injury between 19% and 79%, which is variable due to the ambiguity in defining an injury, the difference in study populations, and follow-up periods.[21] Running is one of the most common sport activities to cause injuries of the lower back and leg.[21] Poorly perfused tissues, such as ligaments, tendons and cartilage, are at a higher risk of injury as they adapt more slowly than muscles to an increased mechanical load.[21]

Treatment of sports injuries

Initial treatment

The treatment of injuries in runners should combine five strategies which are aimed at treating the present injury as well as preventing its recurrence or the occurrence of a different injury.[22] Importantly, these strategies do not necessarily infer pharmacological treatment, but rather non-pharmacological measures. The five strategies are 1) appropriate medical care, 2) athlete education, 3) cross-training, 4) specific exercise and 5) programmed return to running (Table I).[22]

Pharmacological treatment

The World Health Organization's three-step pain ladder determines the appropriate pharmacological medical care depending on the level of pain experienced on a ten-point scale.[28] There are several analgesics and anti-inflammatories, which are commonly used to treat pain and inflammation, such as NSAIDs (e.g. ibuprofen and celecoxib) and opioids (e.g. codeine and tramadol), as single agents or in combination.[3] The most commonly used analgesics and anti-inflammatories and their associated side effects are discussed in Table II.

Nonsteroidal anti-inflammatories

In the majority of cases, NSAIDs are the drugs of choice for the treatment of sports injuries.[3] The NSAIDs are widely used in sports medicine and are the first line of use to decrease pain, swelling and inflammation caused by a soft tissue injury.[3] The NSAIDs exhibit anti-inflammatory and analgesic effects by reducing PG formation due to inhibition of COX.[13] The NSAIDs are available in

Table I: The different forms of recovery strategies that should be applied concurrently to ensure the healing of an injury and to prevent possible recurrence.

Recovery strategy	Description
Medical care	Basic to all forms of treatment are some types of rest for the injured part, usually ice and aspirin or some form of NSAID.[22] Remedial exercise with some form of stretching and strengthening should be included.[23] Complete rest is not suggested as it will result in musculoskeletal atrophy and impaired function.[22]
Athlete education	The single most important factor in reducing both the incidence and recurrence of injuries to endurance athletes.[22] The athlete must understand the reason(s) for the injury, the treatment plan and how to prevent further injury.[22] Athletes should understand that proper technique, proper progression and age-related considerations are all within their control.[22] Athlete education can be accomplished in conjunction with competitions through pre-race communication, pre-race discussions as well as through articles in popular running magazines.
Cross-training	Cross-training means alternative activity or concurrent training in more than one type of activity.[23] The main benefit of cross-training is the central adaptations (mainly cardiovascular) to training. For an injured runner, cross-training allows for the injury to heal while allowing the athlete to maintain a high level of fitness. However, the peripheral adaptations from running will be lost.[23] Therefore, once the injury is healed, the athlete should gradually reduce the time spent on the alternative activity while gradually increasing the time spent running.[23] Cross-training activities include swimming, pool running (may have carry-over benefits), cycling, rowing or any other activity that reduces eccentric and impact loading.[23]
Specific exercises	Specific remedial exercises should be started as soon as the acute inflammatory stage is past.[24] There should be no pain associated with specific exercise retraining. Stretching exercises should be implemented to develop appropriate ranges of motion since injury to tendons or muscles usually results in scarring and consequent shortening. Stretching should be done when muscle temperature has been elevated by a whole-body warm-up. It has been reported that cold stretches may increase the risk of injury.[25] An appropriate technique would be to stretch for 6 seconds followed by 6 seconds of relaxation, repeated ten times. Eccentric strength training, in which the muscle lengthens against resistance, is helpful during rehabilitation and in treating tendinitis.[26]
Return to training	Since peripheral adaptation is lost, even with cross-training, the return to running should be controlled and gradual. The progression thereof depends on the specific injury and the time taken off. Initially, runners should do 15 minutes of slow running every other day, with 5-minute increases weekly. When 40 minutes of painless running is achieved, the distance can be increased by the 10% rule. By following these guidelines, 80% of runners will be able to return to running within three months.[27]

various formulations, including tablets, creams, ointments, sprays, gels and patches.[3]

The NSAIDs are associated with significant gastrointestinal and renal side effects, among other concerns (Table II).[7] Furthermore, NSAIDs may cause water retention and hyponatraemia, causing them to interact with anti-hypertensive medication.[3] Traditional NSAIDs, those that inhibit both COX-1 and COX-2, are commonly associated with more distributed side effects due to their non-selective inhibition of COX, which includes more severe gastrointestinal side effects.[3] Newer agents, such as the COX-2-selective NSAIDs (COXIBs), are more selective for COX-2 and are effective at decreasing pain and allowing a quicker return to activity and rehabilitation.[29-31] The COXIBs also have a reduced frequency of gastrointestinal and renal side effects.[32] Although traditional NSAIDs and COXIBs have similar efficacy in the clinical setting, COXIBs are a safer choice due to their gastrointestinal safety profile.[32] However, COXIBs are associated with an increased risk of thrombosis (due to the inhibition of prostacyclin), increased blood

Table II: The commonly used oral analgesics and anti-inflammatories and their recommended doses and their commonly associated side effects.[38]

Drug (product example[s])	Recommended dose	Side effects
Aspirin (Bayer Aspirin®)	325 to 650 mg every 4 to 6 hours, with a maximum daily dose of 4 g.	Indigestion, stomach aches and bleeding or bruising more easily than normal.
Celecoxib (Celexib®)	200 mg daily or 100 mg every 12 hours. The maximum daily dose is 400 mg per day.	Stomach pain, constipation, diarrhea, heartburn, nausea, vomiting, dizziness, headache, respiratory tract infection.
Diclofenac (Voltaren®)	50 mg every 8 hours, with a maximum daily dose of 150 mg.	Nausea, vomiting, diarrhea, vertigo, headaches, stomach aches, loss of appetite and mild rash.
Ibuprofen (Deep Relief®)	400 mg every 4 to 6 hours. The maximum daily dose is 3 200 mg (acute) or 2 400 mg (chronic)	Headaches, dizziness, nausea, vomiting and indigestion.
Indomethacin (Arthrexib®)	Immediate release: 25 to 50 mg every 8 to 12 hours. Controlled release: 75 mg once or twice daily. The maximum dose is 150 mg per day.	Stomach pain, diarrhoea, indigestion, nausea and vomiting.
Meloxicam (Loxiflam®)	7.5 to 15 mg once daily. The maximum daily dose is 15 mg.	Diarrhea and indigestion.
Naproxen (Aleve®)	250 to 500 mg every 12 hours (naproxen based) or 275 to 550 mg every 12 hours (naproxen sodium)	Confusion, headaches, ringing in the ears, changes in vision, tiredness, dizziness and rashes.
Paracetamol (Panado®, Dischem Paracetamol®)	Adults: 650 to 1 000 mg every 6 hours with a maximum of 4 g/day Children: 15 mg/kg body weight every 6 hours with a maximum of 60 mg/kg body weight per day.	Nausea, vomiting and constipation.

pressure, oedema and congestive heart failure.[3,32-33] Additionally, COXIBs are more costly, which may be a reason patients opt for traditional NSAIDs.[34]

All of the risks associated with selective or non-selective NSAIDs are a major concern; however, it appears that athletes opt for analgesic use due to their perceptions of improved performance and prophylactic management of injuries.[35] The use and misuse of analgesics is prevalent in sports due to a lack of adequate knowledge of the effects and side effects of these agents.[36] Moreover, the use of analgesics and anti-inflammatories is speculated to delay muscle recovery as the PGs inhibited by drugs such as NSAIDs are important in the turnover of protein for protein synthesis during muscle repair.[3]

When looking at aspirin specifically, analgesic and antipyretic effects appear at doses up to 300 mg, while anti-inflammatory effects occur at higher doses alongside an increased risk for gastrointestinal side effects (e.g. gastric ulcers).[3] Aspirin's use in sports is limited due to its ability to inhibit platelet aggregation, which may increase bleeding,[3] where a single dose of 100 mg aspirin abolishes thromboxane A_2 production by COX-1 on blood platelets, inhibiting blood clotting, which may precipitate bleeding.[37]

Paracetamol

Paracetamol displays both antipyretic and analgesic effects but lacks anti-inflammatory or anti-clotting properties as it specifically inhibits the COX-3 isoform (predominantly found in the central nervous system and in the heart).[3] The use of paracetamol in acute sports injuries is reported to be safe up to a 3 to 4 g/day dose, with the incidence of side effects being similar to that of the placebo.[39] However, an overdose of paracetamol can cause severe hepatic necrosis.[40]

Opioids

Opioids mimic the actions of endogenous opioid peptides by interacting with the μ, δ and κ receptors.[41] These receptors are coupled to G_i proteins, which close N-type voltage-operated calcium channels and open calcium-dependent potassium channels, resulting in hyperpolarisation-induced reduction of neuronal excitability.[41] Activation of the opioid receptors also decreases cyclic adenosine monophosphate (cAMP) production, which modulates the release of nociceptive neurotransmitters such as substance P.[41]

Codeine, a potent opioid analgesic,[39] is often used in combination with aspirin or paracetamol.[30] However, it is reserved for more severe pain due to its addictive properties.[39,42-43] Tramadol, also an opioid, is effective in the treatment of neuropathic pain,[12] but it has been suggested that it may have a lower efficacy and a greater incidence of side effects compared to the COXIBs when treating lower back pain.[44] The use of tramadol in sports medicine is more appropriate in severe injuries when additional analgesia is needed.[3]

The use of analgesics in runners

Athletes, including cyclists, runners and triathletes, have indicated the use of NSAIDs prior to, during and after sporting events.[9] Furthermore, 33% of runners use analgesics to aid recovery from an RRI.[45] The use of analgesics in runners ranges from 64 to 71%.[5,9] Moreover, 35 to 57%, 11 to 56%, and 56 to 80% of runners take analgesics prior to, during, and after a run, respectively.[5-6,9] Athletes competing in ultra-distance marathons are more likely to use NSAIDs during the event than those running marathons and half-marathons.[6] The most commonly used analgesics include NSAIDs (ibuprofen, diclofenac, naproxen and celecoxib and aspirin) and paracetamol.[4,6] Myprodol®, a combination of paracetamol, ibuprofen and codeine, is commonly used by runners during a run.[5] Some runners believe that taking a single analgesic is not effective in relieving muscle and joint pain. Hence, they opt for the use of a combination of analgesics.[5] For example, runners may take Myprodol® in combination with diclofenac, or some runners take diclofenac and ibuprofen in combination during a run.[5] The use of analgesics in runners is significantly higher in those individuals who reported a previous RRI,[5] where a RRI is a three-fold predictive factor for use of analgesics compared to other factors.[5] Concerningly, runners have also reported taking excessive doses of NSAIDs available over-the-counter.[4] In one study, diclofenac was taken at a dose of > 100 mg, whereas ibuprofen was taken at 800 mg (twice the recommended daily dose).[4] Approximately 3.4% of runners have reported exceeding the recommended daily dose of NSAIDs.[1] In 2009, it was reported that analgesics were the most common category of drug in acute overdose in adult patients (10%).[46] Paracetamol alone or in combination accounted for 42% of acute overdose cases for the analgesics group, and NSAIDs accounted for 33% of cases.[46] Ibuprofen is the most common NSAID taken in cases of overdose (81%) followed by naproxen (11%).[46]

Analgesics are mainly accessed over the counter by 90% of runners, with 45% doing so without the recommendations of a healthcare professional.[5] Pharmacists are only responsible for 25% of the recommendations, with friends and family being responsible for 19%.[5] In South Africa, analgesic use appears to be increased in runners as they believe that many other runners are using them.[5] There is limited knowledge about analgesics and the associated side effects thereof,[4-5] where approximately 93% of runners are not aware of the risk of using analgesics in connection with endurance sports.[4] Furthermore, South African-based runners have good attitudes towards the use of analgesics but lack knowledge of their specific side effects, effects and drug interactions.[45] This then translates into bad practices regarding analgesic use.[45] For example, in one study 68% of South African runners used analgesics in running despite showing good attitudes towards the use thereof.[45] It has been shown that being part of a sports club is a predictor of self-medication.[45]

The incidence of side effects from analgesics is significantly higher in marathon runners compared to half-marathon runners (18% vs 7%).[4] The incidence of analgesic-related side effects is 4 to 10

times higher when compared to a control cohort during a run.[4] Common analgesic-related side effects include gastrointestinal cramps, haematuria and cardiovascular events (arrhythmia and palpitations), with gastrointestinal cramps and cardiovascular events being the most frequent.[4] Moreover, gastrointestinal cramps in runners taking analgesics are frequently blamed for race withdrawal.[4] Increasing the dose of analgesics used during a race increases the onset of side effects by three-fold.[4] The drug-related incidence of side effects during a race is most frequent with ibuprofen, aspirin and diclofenac.[4] Aspirin has been associated with numerous cases of gastrointestinal and kidney bleeding (49% of individuals reported this occurred during a race when aspirin was taken at high doses).[4] In some cases, side effects experienced from analgesic use during a marathon required hospital admittance.[4] Interestingly, it has also been reported that NSAID use decreases the amount of collagen synthesised after prolonged running.[47] It was found that twice daily ingestion of 100 mg of the NSAID indomethacin significantly reduced the levels of pro-collagen type I N-terminal propeptide, an important peptide in collagen turnover, in the patellar tendon after a 32 km run compared to the control group.[47]

Recently, there has been controversy in the world of endurance sports when the use of ibuprofen was banned in the Ultra Tour de Mount Blanc, one of the world's leading sports events, due to "negative health risks".[48] Studies reported that kidney injury was frequent in ultra-marathon runners with an association between NSAID use and acute renal injury/failure.[49] The use of NSAIDs was present in approximately 79 to 80% of acute renal failure cases.[50] The NSAID indomethacin has been shown to cause a significant reduction in renal blood flow during exercise and post-exercise, which caused a marked elevation in the mean arterial pressure and renal vascular resistance.[51] Exercise increases the amount of vasoconstriction-inducing hormones and renal sympathetic neuronal activity, which is modulated by renal prostaglandins.[51] Thus, blocking the production of these prostaglandins by using NSAIDs results in reduced renal blood flow.[51] Interestingly, this phenomenon only occurs during exercise and not under normal/basal conditions.[51]

Historically, the Comrades Marathon reports the highest incidence of acute renal failure in any sporting event in the world (2/10 000 runners).[50] The highest reported incidence of acute renal failure of 10/10 000 runners was in the 1986 Comrades Marathon.[50] In such instances, the cases vary from unrecognised failure that persists for around ten days after the Comrades Marathon to significant renal damage requiring extended hospitalisation and peritoneal dialysis.[50] The reason for this occurrence is deemed to be due to dehydration secondary to inadequate fluid intake and/or diarrhoea, vomiting, rhabdomyolysis and the use of analgesics (such as paracetamol and NSAIDs).[50] In a case study on four individuals who were admitted to the hospital for acute renal failure after having run the 2010 Comrades Marathon, it was found that three of the four individuals ingested NSAIDs during the race, whilst the fourth individual ingested a muscle relaxant.[50] The patients all presented with hyponatraemia one to four days after the race finished.[50] The authors suggested that the hyponatraemia was secondary to acute renal failure (ARF), which produced dilutional hyponatraemia secondary to protracted anuria/oliguria.[52] It was suggested that rhabdomyolysis, exercise-induced hyponatraemia and NSAID use may have caused the ARF.[50] However, more research needs to be conducted on this cohort of athletes to identify the factors placing these athletes at risk of life-threatening medical complications such as exercise-induced hyponatraemia and ARF.[50]

Conclusion

Findings reveal that NSAIDs are an easily accessible drug for runners to prevent or treat RRIs or exercise-induced inflammation and pain; however, many runners do not understand how these drugs exert their effects and what risks may be present. Importantly, there is a lack of knowledge of the side effects associated with such drugs in the context of endurance running. Athletes tend to use higher doses of analgesics, particularly NSAIDs such as ibuprofen and diclofenac, than those recommended and may engage in polypharmacy. The analgesics are obtained over-the-counter without the recommendation of a healthcare professional.

While injury is a predictor for use of NSAIDs, runners appear to be using NSAIDs to participate in events, to push through injuries by increasing pain tolerance and to deal with post-event soreness. The high use of NSAIDs without full knowledge of side effects, contraindications or cautions for use is a major concern. The lack of evidence for the benefits of using NSAIDs in exercise means that some runners are making poor benefit-harm decisions. Recreational runners appear to have an unmet need for more information on NSAIDs, which can be filled out by organisers of sports events or healthcare professionals (such as pharmacists, physiotherapists, sports practitioners, and biokineticists). The high use of NSAIDs before and during endurance running events is concerning, given the greater physiological stresses associated with these events. The organisers of endurance running events, as well as popular running media platforms, should consider providing athletes and coaches with evidence-based advice on the use of NSAIDs, as well as tracking systems for adverse effects experienced during events.

Conflict of interest

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The contribution of pharmacists in managing the disease burden in South Africa: a SAAHIP at SAPHEX report

Nhlanhla G Mafarafara, Seshnee Moodley, Rofhiwa Mulibana

Introduction

The Pharmacy Show 2024 hosted at the Sandton Convention Centre from 13 to 14 March 2024 brought thousands of "industries most influential speakers" spread through parallel conferences taking place amidst 200 hundred exhibitors.[1] The South African Association of Hospital and Institutional Pharmacists (SAAHIP), hosted a three-part Hospital Pharmacy Show covering the following practice areas: human resources for pharmacy; multidisciplinary collaboration and wound care. Sessions were designed with the background that pharmacists are the most accessible healthcare professionals to the public.

This article provides insight highlights from the three sessions as well as one other panel conversation on Health Technology Assessment.

Human resources for pharmacy

This session was chaired by SAAHIP President, Nhlanhla G Mafarafara featuring Andy Gray, senior lecturer at the University of KwaZulu-Natal, as the invited guest speaker. A comprehensive, safe, and effective pharmaceutical service and delivery of effective universal health coverage requires adequate numbers of appropriately trained and motivated pharmaceutical personnel, across a range of professional and support categories. South Africa has an absolute lack of human resources for health, exacerbated by unequal distribution between public and private sectors and between urban and rural settings.[2]

The objectives of this session were:

- To review the currently available data on the number and distribution of pharmaceutical personnel in South Africa.
- To relate the available data to those from the international community.
- To explain how human resources for health affect the ability to deliver effective universal health coverage, using the UHC Service Delivery Index.
- To explore the health systems challenges facing South Africa as it relates to human resources.

There are just over 16 856 pharmacists registered with the South African Pharmacy Council, 36% of which is in the Gauteng Province.[3]

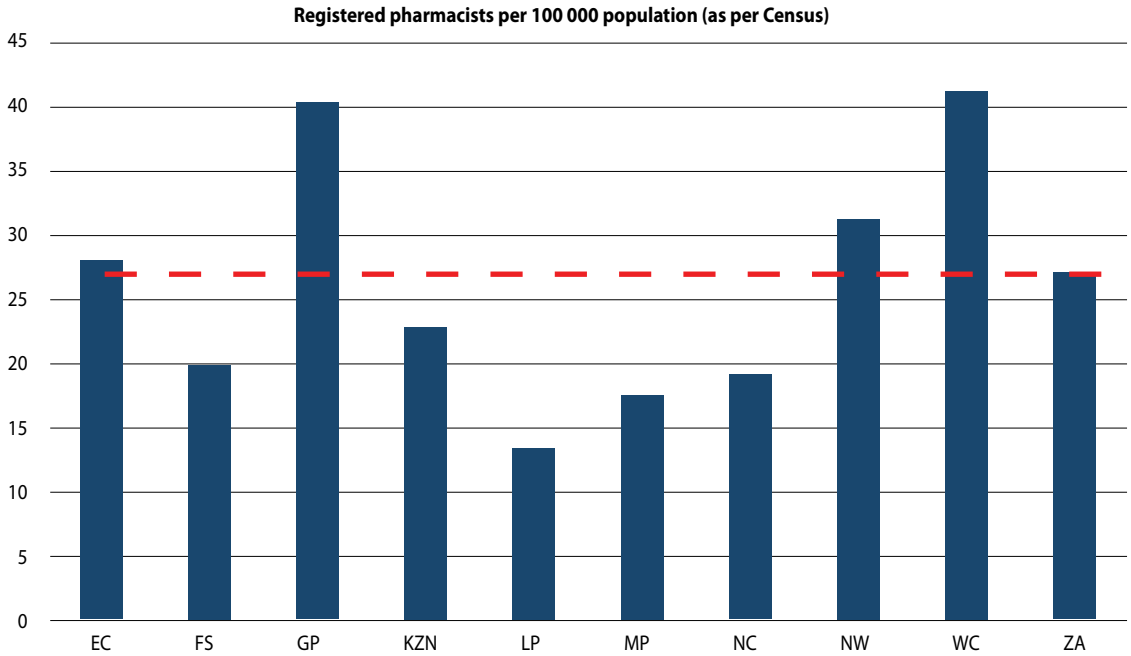

Figure 1: Registered pharmacists per 100 000 population[6]

All Western Cape districts are above average, and all KwaZulu-Natal districts are below average of pharmacist per 100 000 population. The national average is 31/100 000 (Figure 1). There is also missing data on the number of pharmacists who are practising or have retained their registration as practising but have already emigrated elsewhere. Furthermore, since the introduction of occupation specific dispensation (OSD)[4] in 2009, pharmacists experienced the highest growth of 186%, while professional nurses recorded the lowest growth at 29% (Figure 2). Despite this sharp increase, the NDoH's 2030 Human Resources for Health Strategy (2020) suggests that "serious PHC shortages for healthcare personnel, including pharmacists and pharmacy assistants, will worsen by 2025 if nothing is done".[5]

We cannot build an equitable health system and not engage the full range of the pharmacy workforce. South Africa needs to join the global commitment to workforce transformation and that there is "no health without a pharmacy workforce" and close the widespread human resource inequalities if universal health coverage goals are to be realised.

Other opinions raised during the debate

- Most patients in public sector primary healthcare facilities are not getting pharmaceutical services, they receive medicines.
- There is a need to close the patient safety and rational medicines use gap.
- Professional organisations need to increase their advocacy for human resource for pharmacy.
- Service delivery models for NHI need to be redefined to suit the broader pharmacy environment.
- There should be routes of entry and practice that are not based on all-or-nothing model in the envisaged pharmacy specialisation environment.
- Shortage of pharmacy workforce and increased pharmacy workload could/are a threat to adequate pharmaceutical service.

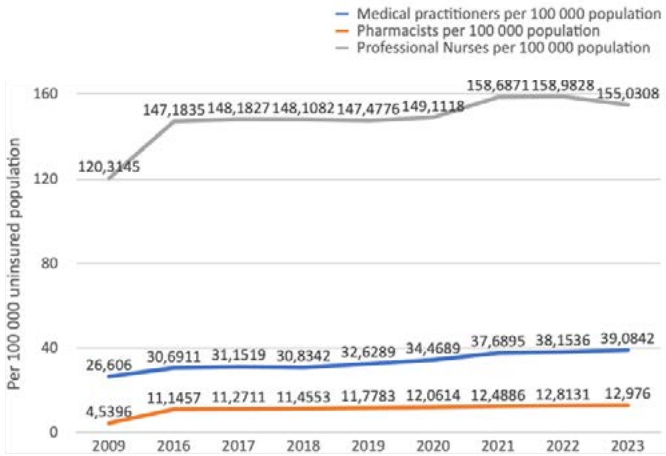

Figure 2: Ratio of professional nurses, pharmacists, and medical practitioners per 100 000 uninsured population, March 2009–March 2023
Source: PERSAL. Published in District Health Barometer, 2022/23[iii]

Multidisciplinary collaboration

A multidisciplinary team (MDT) involves a range of health professionals working together to deliver comprehensive patient care. The MDT offers benefits such as improved health outcomes, patient satisfaction, efficient use of resources and enhanced job satisfaction.[7]

In this session, chaired by Rofhiwa Mulibana, a Senior Pharmaceutical Services Technical Specialist at Right to Care, featuring two invited guests looked at two learning outcomes:

- How healthcare professionals from a range of disciplines can work together to deliver comprehensive care that addresses as many of the patient's needs as possible.
- How healthcare professionals can collaborate with Traditional Health Practitioners for better health outcomes.

The growing use of traditional/herbal medicines – what pharmacists need to be cognisant of

This presentation was delivered by Mamolefe Selokela, who is the African Traditional Medicines (ATM) Program Manager for Mpumalanga Province Department of Health. Pharmacists need to have a better understanding of herbal and traditional medicines, which were referred to as health practices, approaches, knowledge, and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques, and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain a person's well-being.[8]

In the process of rethinking about the potential contribution of ATM and traditional health practitioners (THP) to healthcare coverage, health policies should be geared towards collaboration between or integration of Western and African traditional medicines.

Challenges related to ATM and THP

- Policy and Regulations: there is limited enforcement of regulations for THPs in some countries.
- Limited collaboration between THP and conventional medicines.
- Literacy of THPs: the majority of THPs did not receive formal education which hinders their integration in mainstream health in line with the 2018 Astana Declaration.[9]
- Inexplicable practices: the scientific basis of how spiritual THPs practice is inexplicable according to current scientific knowledge.
- Intellectual property rights: the lack of internationally agreed framework and national guideline on the protection of intellectual property versus the THP's protection of their therapeutic knowledge.

The NDoH, guided by the World Health Organization has made recommendations to include traditional medicines in the national health system, regulate ATM practice, develop a national pharmacopoeia of ATM, establish an appropriate journal on ATM to deal with issues and trends on ATM, establish an Inter-ministerial Committee on ATM, developing and institutionalising ATM, develop protocols and guidelines for communication on ATM to all sectors, and sensitisation of the society on ATM through campaigns for recognition and legitimacy of ATM.[10,11,12]

The pharmacist as the custodian of OTC codeine: ensuring safe and responsible use

Delivered by Rubina Shaikh, a lecturer in the Division of Pharmacy Practice, Department of Pharmacy and Pharmacology at the University of Witwatersrand. The role of pharmacists as the custodian of medicines is referenced in the Good Pharmacy Practice Guidelines (GPP) and defined in the Scope of Practice of a pharmacist within these Guidelines.[13] The medicine related needs that can arise with codeine use were highlighted as well as the regulatory landscape, accessibility of codeine-containing products and the implications for patient safety. Pharmacists can improve communication strategies, develop their clinical knowledge of codeine misuse, familiarise themselves with the latest trends in recreational use and implement pharmacovigilance monitoring systems to address codeine misuse.

Other strategies and innovations include policy reforms, use of technology, educational and drug monitoring programmes. A major challenge facing policy makers is how to ensure the availability of codeine-containing products for those with legitimate therapeutic need whilst reducing the consumers' risk of misuse and dependence. Therefore, it is of utmost importance that intervention strategies and policies are implemented to ensure patients are provided with equal balance of access to these medicines and protection.

Pharmacists are required to work in a multidisciplinary team more often and their role in a multidisciplinary team is to optimise patient and rational use of medicines. Integration of pharmacists into MDTs has been shown to have a positive effect in several clinical, pharmaceutical, and financial indicators.[14]

Pharmacists in wound care

Wound care took centre stage in the conclusion to the SAPHEX SAAHIP session. The final session was chaired by Dr Seshnee Moodley (SAAHIP Vice-President) and included two very knowledgeable speakers, Dr Sybil Seoka and Sister Angela Gordon-Davies. The session speakers focused on the pharmacists' involvement in wound care, they also highlighted that working in MDTs is vital, and necessary referrals is often the key to optimising wound care healing especially if patients are suffering from chronic wounds. Pharmacists play a vital part in the patient care chain in both community pharmacy setting or for ambulatory patients in a hospital setting.

The pharmacist needs to be more aware of wound dressings and antibiotic therapy when advising therapy to patients. Some dressings also contain active pharmaceutical ingredients. These dressings must be monitored appropriately and there should be constant and continuous quality checks done on them. However, often this is not adhered to and leads to an increase in expenditure.

Other areas to be looked at include:

- Storage of the wound dressings
- Efficient procurement
- Prudent procurement (waste avoidance)
- Pharmacists' clinical involvement

The NHI Health Technology Assessment

In an addition to this, Andy Gray chaired a session on Health Technology Assessment. This was a moderated panel discussion with three pharmaceutical policy specialists from the Essential Drug Programme (EDP) in the Affordable Medicines Directorate (AMD), NDoH (NDoH): Dr Janine Jugathpal, Ms Maropeng Rapetsoa and Dr Jane Riddin. The aim was to enable attendees to gain new insights into the planned application of health technology assessment (HTA) processes in the selection of medicines, supporting decision-making for essential medicines in a resource-constrained fiscal environment.

Currently, the NDoH (EDP) co-ordinates the development of the national Essential Medicines List (EML) and Standard Treatment Guidelines (STGs) through the ministerially appointed National Essential Medicines List Committee (NEMLC) and Expert Review Committees (ERCs). The EML is an explicit list of medicines that should be available in the public health system. STGs provide guidance to healthcare professionals on the rational use of medicines. Over the past two decades, South Africa has incrementally increased the use of HTA processes in selecting essential medicines in the public health sector. The selection of essential medicines and the development of STGs is based on an assessment of evidence for efficacy, safety, cost-effectiveness, and affordability, generally compared to the current standard of care. HTA has been defined locally as the use of "scientific evidence, interpreted through the lens of social and scientific value judgements, to inform an accountable approach to making health technology access and resource allocation decisions".[15] South Africa is expected to rely on HTA in the design and operation of National Health Insurance (NHI), as it seeks to deliver universal health coverage. Although HTA has been explicitly mentioned in the NHI Bill, the specific arrangements, and structures to be created are yet not identified. There is at present no formal national HTA institution in South Africa.

The panel discussion covered the current NEMLC processes for medicines selection, including the use of an explicit evidence-to-decision (EtD) framework, the lessons learned during the COVID-19 pandemic, and the current plans to formalise HTA within the NHI structures. The panel also identified areas of concern, where detailed planning has yet to be conducted, including the provisions for the pricing of medicines to be procured or reimbursed under NHI, the future of the state tender system, as well as the potential implications for the Central Chronic Medicines Dispensing and Distribution (CCMDD) programme.

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Withdrawal Note

Medpharm Publications reports the withdrawal of the following article:

Impact of pharmacist-led interventions in improving adherence to glaucoma medications in the geriatric population

With the DOI: https://doi.org/10.1136/ejhpharm-2021-002788

At the time of republication the applicable permissions were not in place and the publisher therefore wishes to withdraw this article. The original article can be viewed here:

http://ejhp.bmj.com/content/28/e1/e191

Medpharm Publications

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News

Success story of young pharmacists

Thuto Bodibe

Introduction

Dear Fellow pharmacy community, welcome to this exciting interview with this vibrant young pharmacist. In this series of interviews, we will be having discussions with pharmacists who have less than 5 years' experience post their internship regarding their success stories, "their" being the operative word. We want to get you our fellow pharmers stories of young pharmacists who made their mark in the profession according to their standards.

Thank you to the South African Pharmaceutical Journal (SAPJ) for requesting these interviews in order for us to showcase the great work that is being done out there. Visit SAPJ online for the latest issue of the journal for stories like this and all your clinical reviews on self-medication topics, information on prescription medication and all other essential information for referring customers for early medical attention should it be required.

My name is Kesentseng Jackson Mahlaba; I am a pharmacist and a lecturer at the School of Pharmacy at the Sefako Makgatho Health Sciences University (SMU). I have been in the profession for over 15 years' in institutional pharmacies and over eight years in academia.

I am a health advocate in vaccine hesitancy, medicine management and rational medicines use in order to improve access to and adherence to medicines by patients and communities at large. I am the current Chairperson of the Northern Gauteng branch of the South African Association of Hospital and Institutional Pharmacists and a scientific advisor to the South African Vaccination and Immunisation Centre at Sefako Makgatho Health Sciences University.

Meet Thuto Bodibe

1. ***Introduce yourself to the readers of SAPJ so that they have a broader understanding of your journey to this point.***

   My name is Thuto Bodibe, a 28-year-old pharmacist from Soweto. Currently, I am practising at Stanza Bopape CHC, a Community Health Centre (CHC) in Mamelodi, named one of the busiest clinics in Tshwane.

2. ***Where did you study pharmacy, and what made you choose pharmacy as a career choice?***

   I studied both my undergraduate BPharm degree and postgraduate MPharm degrees in Public Health Pharmacy and Management at SMU. After completing matric, I was determined to pursue a career in healthcare in order to help people, but I was unsure with regards to the discipline to choose and also lacked funds to apply to various universities to improve my chances to secure space. This resulted in me spending a year at home. However, during that time, I underwent career counselling and explored various courses; this is where I truly met pharmacy. I decided to apply at the University of Limpopo, Medunsa campus, now SMU. Mind you, I had only applied to one university and fortunately I was accepted to begin my studies in 2015.

3. ***Most, if not all students, experience obstacles during their study period. What were some of those obstacles for you and how did you go about overcoming them?***

   During my undergraduate studies, I really cannot recall many obstacles, aside from grasping certain concepts and the way of learning at university. This put tremendous strain on me as I had to put in extra effort and time to ensure I passed. However, resilience was my guiding force. Also, I was fortunate to have a supportive network of friends and some academic staff who ensured that no student was left behind. Additionally, we had mentors assigned to us to help navigate the programme. All this support played a role in the award I received for being one of the top two learners in my class in my final year of undergraduate studies.

   Transitioning to my postgraduate masters studies, the first year was challenging but manageable. I successfully balanced my responsibilities as a student and an academic intern. However, the second year brought unforeseen challenges with the onset of the COVID-19 pandemic. This period affected most students' mental health, myself included. Just after I completed my research proposal, I was informed that I couldn't proceed with data collection as my study required direct client contact. This setback necessitated a protocol amendment and an extension of my academic internship. Despite these challenges, I had unwavering support from my supervisors, other academic staff and a few friends who kept me going. Ultimately, I achieved a distinction in my dissertation after examination.cdfx

4. ***If you could highlight one thing that kept you motivated during your studies, what would it be and why?***

The fear of failure served as my driving force. I was terrified of the prospect of failing and returning to poverty in the township where I grew up, without achieving anything. Being the first person in my family to attend university, I felt a profound responsibility to make my grandmother proud. Although the journey wasn't easy, and it continues to pose challenges, I am determined to persevere. It is crucial to never give up, "Whatever the mind can conceive and believe, it can achieve" - Napoleon Hill.

5. ***They say: If you want to go fast, go alone but if you want to go far, go together. During your time at university, who were some of the people who 'walked with you' to get you to the point of graduation?***

I was fortunate to have an incredible group of friends from my undergraduate years who motivated and supported each other. The academic staff members of SMU were also exceptionally supportive throughout my journey. Additionally, I received support from a non-biological family who embraced me as an adult and helped whenever needed. Some of my friends evolved into family, and our bond remains strong to this day. We continue to support each other through thick and thin.

6. ***Coming from an academic environment, how did you experience internship at first, and were you able to see how the BPharm degree prepared you for the practice setting?***

The BPharm programme introduced me to Problem-Based Learning (PBL) as the primary teaching method, this for me was totally a new teaching approach compared to the traditional methods I experienced in high school. In PBL sessions, we were presented with real-world problems or case studies we had to work through in groups to identify solutions. Guided by a facilitator, we honed our critical thinking and problem-solving abilities. This learning approach enabled me to think quickly, creatively, and employed my problem-solving skills effectively, which proved invaluable during my academic internship. Moreover, my undergrad played a significant role in enhancing my confidence, particularly in communication and presentation skills. Weekly presentations and active participation in small group facilitations were integral components of our learning process.

Now my internship required that I apply what I had learned in my undergrad as I had to actively seek solutions to the challenges I encountered. This hands-on experience further strengthened my ability to think on my feet and tackle various situations.

I am profoundly grateful for the opportunity provided by my education, as it equipped me with essential skills that continue to benefit me in my professional endeavours today.

7. ***Since completion of your internship, how did you advance through the pharmacy profession to this point? What posts and positions followed?***

After completing my academic internship at SMU, I embarked on my community service at Tshwane Regional Pharmacy. Subsequently, I seized an opportunity to become the second pharmacist at Stanza Bopape CHC. Initially, during my first year at the clinic, I experienced misalignment in my studies and my practice. Determined to make a difference, I stepped out of my comfort zone and became involved with a programme focusing on adolescents and youth, "*The Adolescents and Youth-Friendly Services (AYFS) programme*". This programme was initiated by the Department of Health, to promote health and well-being of young people aged 10-24 years. This programme was relaunched at our facility in December 2022 with a mission to enhance the health status of young individuals through illness prevention, promotion of healthy lifestyles, and enhancement of healthcare delivery systems. Its objective is to emphasise accessibility, efficiency, quality, and sustainability of youth-friendly health services.

I have been fortunate to be nominated to serve as the chairperson, leading the implementation and promotion of AYFS, a role that is incredibly rewarding as it allows me to actively contribute directly at a micro level of health within our community.

8. ***How do your current daily duties and responsibilities compare to what you envisioned a pharmacist doing when you selected pharmacy as a career path?***

There isn't a significant disparity between my current daily duties and what I initially envisioned a pharmacist's role to be. However, my passion lies in public health related work. I find fulfilment in planning health campaigns, providing health advocacy at schools within our catchment area, and promoting the clinic's services, particularly focusing on prevention methods such as contraception and STI prevention. My primary goal is to make a positive impact wherever possible.

9. ***How would you define 'success'?***

Success, for me, means not just achieving goals but finding fulfilment and meaning in what you do.

10. ***How does your definition of success align or differ from the world's or South Africa's perception of success?***

I think everyone interprets success differently, for me, success doesn't only entail having a lot of money nor does it mean not valuing money. Based on my definition, the alignment comes when I am able to wake up every day and pursue goals that align with my purpose, finding fulfilment and meaning in what I do.

11. ***Tell us what makes your story a success story, from which readers can tap inspiration from.***

I'm not sure if I've reached a point in my career that qualifies my story as a success. However, I firmly believe that anyone striving to achieve their goals must understand that the journey won't be easy. It requires resilience and determination to push through challenges. My continuous willingness to learn and grow serves as my driving force, propelling me forward. I hold onto the belief that I am destined for greatness.

12. Which elements do you think one needs to impact your environment, whether your community, profession, or workplace? Do you believe you have made an impact in pharmacy to date?

I am going to discuss my experience and current workplace. To make a difference, one needs good communication skills, influence on policies, teamwork, and dedication to public service. Periodically, it's crucial to evaluate the effectiveness of existing systems and policies and identify areas for improvement. Additionally, engaging with clients whenever possible is essential.

I believe I have made a modest impact in the field of pharmacy, and with further opportunities, I am confident I can do more. I am passionate about learning more as a pharmacist, in order to contribute towards public health efforts.

13. What is the ONE thing every reader can contribute to make pharmacy a better profession or more valued by our patients?

Prioritising empathy is essential during client interactions. Adopting a compassionate approach fosters trust and enhances the overall perception of the profession.

14. How would you like to be remembered one day?

I want to be remembered as a dedicated pharmacist in public health who made a lasting impact on the well-being of clients, ensuring access to essential medications, promoting health education, and contributing significantly to disease prevention.

Who am I as a Pharmacist in 2024?

Geziena Kruger-Swanepoel
SAAHIP, Northern Cape/Free State Branch

Geziena E Kruger-Swanepoel obtained her BPharm degree in 2007 from the North-West University. In June 2022, she graduated cum laude from the North-West University, Potchefstroom Campus and obtained her Master's degree in Pharmacy Practice. She is currently employed as a Responsible Pharmacist at Jan Kempdorp CHC.

"Being a pharmacist is not just a job to me, it is who I am, it defines me, I cannot stop being a pharmacist. There is no greater feeling to experience or to know that you helped make someone feel better today, empowering them with knowledge about medication."

The evolving role of pharmacist in the current landscape, focusing on personal experiences, challenges, and growth opportunities

In Geziena's experience working in a rural Community Healthcare Centre in the Northern Cape Province, the pharmacist and the pharmacy is the central point where all the prescribers (professional nurses and doctors) come to, for medicine information, medicine supply, information on current treatment guidelines, changes in formulary, and adverse drug reactions reporting.

The pharmacy is also the final stop for most patients entering the facility, and therefore it is the responsibility of the pharmacists to ensure that when dispensing medication, prescriptions are checked for interactions, prescribers adhere to appropriate guidelines and lastly to provide the best pharmaceutical care to the patient. If discrepancies are detected, then it is also the pharmacist's responsibility to engage with the prescriber.

Geziena believes that there is an opportunity for pharmacists to settle into a different, more prominent, and active role as part of the multi-disciplinary team looking after a patient. Pharmacists will, therefore, be placed into a unique role where they can teach, learn, and promote adherence to treatment guidelines, to minimise prescribing errors, antimicrobial resistance and enhance overall patient care. Pharmacists are an integral part of the multidisciplinary team and the positive contribution in sharing their exceptional medication knowledge will be well received.

Throughout her career as a pharmacist in the Northern Cape Department of Health, Geziena has practiced in a Rural Primary Healthcare setting, where she has learned to adapt to very limited resources and to improvise daily by thinking "outside of the box", to ensure quality healthcare is provided to her patients. Her passion is antiretroviral medicines (ARVs), teaching the prescribers the guidelines and the importance of monitoring for ARV resistance.

During the completion of her master's degree in pharmacy practice, which she embarked on part time, she did experience some difficulty in balancing work, home and her studies. However, entering the field of research broadened her vision and helped her to see that there are vast possibilities and opportunities to use her skills in her current role as responsible pharmacist. She has now further been inspired to pursue a possible career in research and pharmacovigilance.

Obituary

Peter Hearn

27 February 1932 – 14 May 2024

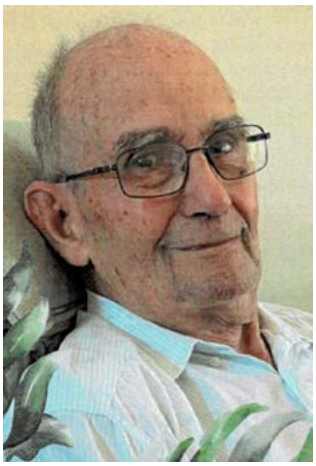
LEST WE FORGET

Our late colleague, Peter Hearn, was born in Cape Town, moved first to Port Shepstone to attend primary school, and then to Pietermaritzburg the year before he enrolled at Maritzburg College. He reached the pinnacle of his career when he was appointed Director of Pharmaceutical Services in the National Department of Health, Pretoria in 1989.

After matriculating from the Maritzburg College in 1948, Peter embarked on his career in pharmacy by doing his apprenticeship in the Pietermaritzburg pharmacy owned by Archie Allen. He obtained his Diploma in Pharmacy after completing the academic course at the Durban Pharmacy School in 1953.

He returned to Pietermaritzburg where he managed Stephenson's Pharmacy until he opened his own pharmacy, Hearn's Pharmacy, in Oribi Road, a few years later. In 1968, he sold this pharmacy but continued as its managing director until 1971, when he commenced work as a pharmacist at Edendale Hospital, a State Health hospital at that time. He was promoted to Senior Pharmacist in 1973 and in 1976 he was promoted to Principal Pharmacist in the same hospital. In 1981, Peter was transferred to the Department of Health's Head Office in Pretoria where he was appointed as Deputy Director of Pharmaceutical Services in 1983. In 1989, he was promoted to Director. On his retirement towards the turn of the century, he and his wife returned to their hometown of Pietermaritzburg, where he continued his professional life for several more years, as a part- time pharmacist at a veterinary supplies wholesale establishment.

There was much more to Peter's life than being a successful pharmacist. He was a committed member of the South African Association of Hospital and Institutional Pharmacists (SAAHIP). When the Inaugural Meeting of the KwaZulu-Natal Branch of SAAHIP took place in Pietermaritzburg on 18 October 1979, Peter was elected as its first chairman. He remained chairman until he left Pietermaritzburg in 1981, having been transferred to Pretoria. On 8 November 1980, at SAAHIP's Annual General Meeting (AGM), he was elected as the Vice-Chairman of the Executive Committee and at the AGM held in 1982, he was elected President, an office he held for three successive years. He was also honoured by being elected a Fellow of the Pharmaceutical Society of South Africa in 1984. In addition, Peter was also a member of the South African Pharmacy Council from August 1986 to December 1993, for which service he was awarded a certificate for his loyal and unselfish service.



He probably experienced the highlight of his career on 30 March 1995, when he attended a conference on board Her Majesty's Yacht Britannia, berthed in Cape Town. He was one of 120 guests who were invited by British Means Business, a trade initiative backed by the United Kingdom Department of Trade & Industry and Foreign & Commonwealth Office. The guests comprised prominent persons active in the field of healthcare, such as doctors, both private and employed in hospitals, specialists in the various medical fields, university professors, and members of the pharmaceutical industry. Peter Hearn attended in his capacity as Director of Pharmaceutical Services.

Peter was in the South Africa Police Reserve for many years, where, as a pharmacist, he helped educate the force in the nature of the then developing illegal drug trade, and in the identification of many different kinds and forms of narcotics and other illegal stimulants.

Peter dedicated many years to his beloved Scoutholm, the 3rd Maritzburg scout troop, where he helped to develop and nurture hundreds of young men. The troop became the largest and most successful troop in South Africa for many years, and a measure of its success and meaning for those young men is the fact that Peter persuaded sixty to seventy of them over the years to attend the meetings every Friday night.

Peter had many interests in life, besides pharmacy. He enjoyed being busy in his workshop, where he tackled any job, such as taking apart the gearbox of his truck, building a crib for his children, and doing French polishing, a pursuit requiring many hours of dedication and patience to get right. He also won Springbok colours for his aero-modelling and he represented South Africa in Sweden at the world championships.

Peter was also keen on sports and the outdoors, and he spent many hours hiking in the mountains with his family. He played and refereed rugby, played badminton, water polo, he wrestled, golfed, loved body surfing, water-skied, and was a keen powerboat racer. With the help

of a couple of close friends and his brother-in-law, he built his boat "Water Witch" and at one time he was the commodore of the power-boat club.

Peter also had a keen interest in wildlife, and at one time bred puff adders in captivity. He and a friend collected the venom and supplied the South African Institute of Medical Research (later known as the National Health Laboratory Service) with this venom that was used to produce antivenom. This project was abandoned after a few years, because his wife considered the snake pit hazardous to the safety of their young, inquisitive children. The reptiles were then donated to the now closed Fitzsimons Snake Park in Durban.

When Peter celebrated his 90th birthday in 2022, the past chairmen of the KwaZulu-Natal Inland branch of SAAHIP, and the current committee members, arranged a surprise birthday party in his honour. The event was enjoyed by all present, and, besides being a birthday celebration, it provided the younger pharmacists an opportunity to meet a stalwart of the organisation, as well as those pharmacists who had previously served the organisation.

Foremost, Peter was a devoted husband, father and grandfather. He is survived by his wife, Cherry, to whom he was happily married for sixty-seven years, a son, two daughters, and three grandchildren.

Susan Buekes

sapj

CPD questionnaire • May/June

Update on the pharmacological management of neurodegenerative diseases: Alzheimer's disease

1. Which of the following neurodegenerative diseases is the most common?

a Parkinson's disease
b Huntington's disease
c Alzheimer's disease
d Motor neuron disease

2. The only drug combination approved by the US-FDA for the treatment of Alzheimer's disease is:

a Aducanumab and memantine
b Galantamine and rivastigmine
c Donepezil and rivastigmine
d Donepezil and memantine

3. Which of the following drugs is a monoclonal antibody targeting beta-amyloid (Aβ) proteins?

a Memantine
b Lecanemab
c Rivastigmine
d Donepezil

Management of allergies and sinusitis

4. Allergic diseases are a group of _____, _____ disorders that occur because of the immune system's activation by _____.

a Chronic, infectious, viruses
b Acute, infectious, bacteria
c Chronic, inflammatory, allergens
d Acute, inflammatory, injury

5. Secretion of cytokines will stimulate cells to produce IgE antibodies and proliferate eosinophils, mast cells and neutrophils. This will result in:

a Vascular constriction, bronchodilation and infection
b Vascular leakage, bronchoconstriction and inflammation
c Vascular dilation, bronchoconstriction and shock
d Vascular dilation, bronchodilation and inflammation

6. Intranasal corticosteroids have shown efficacy against both chronic rhinosinusitis and acute rhinosinusitis. They are intended for short term use to prevent side effects such as:

a Atrophy of nasal mucosa
b Weight gain and increased appetite
c Hyperglycemia
d Suppression of immune system

7. Antihistamines are the first-line therapy for treatment of acute rhinosinusitis. The second generation of antihistamines, e.g. cetirizine and loratadine are preferred, because:

a They have more anti-inflammatory properties to reduce swelling in the nasal mucosa
b They are more effective in atopic patients with symptoms like rhinorrhea.
c They cross the blood-brain barrier, increasing efficacy centrally.
d They have higher affinity for histamine receptors, with less sedative anticholinergic effects.

The misuse of analgesics and nonsteroidal anti-inflammatories in runners

8. Which poorly perfused tissue is at a higher risk of injury as it adapts slowly to an increased mechanical load?

a Muscle
b Tendons and ligaments
c Cartilage
d Adipose tissue

9. Which sub-group of runners are more likely to use NSAIDs during an event?

a 5 km runners
b 10 km runners
c Marathon runners
d Ultra-marathon runners

10. Which is the most common NSAID taken in cases of overdose?

a Ibuprofen
b Diclofenac
c Naproxen
d Celecoxib

11. What is one major risk of using analgesics and anti-inflammatories such as NSAIDs during a marathons and ultra-marathons?

a Decreased performance
b Acute renal failure
c Cramps
d Seizures

The answers for these CPD questions will be in the upcoming issue of the SAPJ.
This activity can contribute towards your CPD compliance.

CPD answers • March/April

1. a 2. d 3. a 4. b 5. a 6. d 7. d 8. d

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Congress theme:
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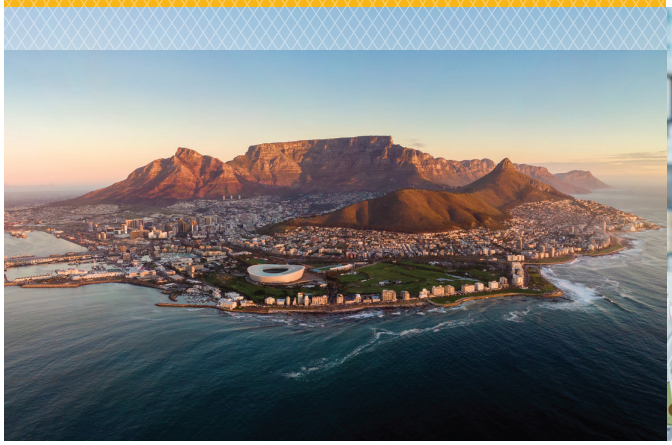

The potential for innovation in health care is vast and holds the promise of revolutionising the way we prevent, diagnose and treat diseases. With advancements in technology, data analytics and interdisciplinary collaborations, the healthcare industry is poised to undergo significant transformation in the coming years.

Pharmacists are pivotal for healthcare innovation across all settings due to their medication expertise, patient access, medication management responsibilities, collaborative nature, public health-impact, technology adoption and contributions to continuity of care.

Their involvement ensures that innovative practices are integrated into everyday healthcare delivery, leading to improved patient outcomes, enhanced safety and advancements in health care as a whole. By embracing these advancements, we can envision a future where health care is truly patient-centric, preventive and sustainable.

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