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Africa HEALTH



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Gastroenterology in the elderly

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Learning the lessons

There is a vibrant discussion taking place at the moment about how African scientists and researchers can be encouraged to increase and improve their outputs. I completely back the argument. But often frontline health workers (physicians, nurses, paramedicals) are also brought into the equation with criticism that they also are not doing enough research. At the risk of upsetting a few, I find myself repeatedly re-hearing the comments of a leading academic at a medical education conference in Harare earlier in the year. 'I'm not sure doctors should do research', he said, 'they should concentrate on teaching'.

The academic in question was Kevin Marsh, Senior Advisor to the Nairobi-based African Academy of Science when addressing the MEPI (Medical Education Partnership Initiative) conference. And he has a point. Pushing back the barriers of knowledge is vitally important, but can be a little self-indulgent when set against the huge responsibility of nurturing the next generation of doctors or nurses or anaesthetists coming through the ranks.

Could it be that the 'teaching lobby' needs to get itself organised! It is losing out on the chatlines of international health to the very well-meaning and well-intentioned research lobby, which is trying to see how Africa's voice and Africa's ailments (from non-communicable diseases to neglected diseases) can gain a greater platform and voice in the international arena.

Everyone in medical practice needs to remember that they were once students of their trade. There will be favourite teachers, and despised ones too… but the overwhelming memory will be for those who made a positive impression or impact on the up-and-coming rookie.

Do enough senior professionals give enough back to the new generation now? I don't know and maybe it is an area that needs a little bit more light shedding on. The research agenda explores all angles, maybe time the teaching agenda caught up a bit of lost time?

As I write, Sierra Leone has been declared free of Ebola. It has been a long slog, and one that has not been without its financial controversies involving both the Ministry of Health and Ministry of Defence in Freetown, but celebrations all round. This is a huge moment after a very difficult couple of years, which has seen a huge loss of life from Ebola (not least among the health professions who recorded 221 losses), but an even greater loss from malaria, measles and diarrhoel diseases as the health system collapsed under the pressure of the communicable and frightening Ebola Virus. There is a huge regeneration and restructuring programme that now needs to be put in place to regain the lost ground against these historic curses. Fingers crossed that sometime in December, Guinea will also get the all clear (they are counting down the days now since their last case), and Ebola in West Africa will be consigned to history, or at least this deadly outbreak.

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Medical attention for the poor



Shima Gyoh traces the advent of user fees in the Nigerian health service, its effect on hospital attendance, and the remarkable volte-face of leading agencies who now realise how wrong they were. Read on

Cancer of the breast often starts as a relatively painless lump, and, near the skin, may break through and look like a boil. In Africa, the women consult their usual traditional medical practitioners who try local herbs, dressings, and administer concoctions and spiritual incantations, but the lesion won't go. Patients are eventually reduced to severe anaemia and weakness as the tumour disseminates throughout the body. They are often brought to hospital only when death is imminent and the tumour inoperable.

Distressed by this, I started a campaign in Kaduna in the early eighties to educate women on the condition. The Rowntree Foundation (UK) donated a video camera, and the Nigerian television kindly broadcast many of our recordings, lectures and demonstrations conducted in both English and vernacular. We also gave talks to villagers at the huge outpatients' attendances.

The results were impressive. Some enlightened town women came up with tiny lesions they found by self-examination. Most were benign, but few were malignant and we hoped we had removed them before they had time to metastasise. Villagers began to come at earlier stages of the disease and we were able to attempt either curative operations or do palliative procedures that improved the quality of life even for the worst cases. All treatment was free.

On the political front, Nigeria was under military rule, and under pressure from the World Bank that the government had set the value of the country's currency unrealistically high and should allow it to float in accordance with market forces. The Naira was then almost equal to the British pound at £0.95 and exchanging for almost 3 US dollars. To help the country survive the rough financial weather expected with floating the currency, the Bank offered Nigeria a loan, but with what they called conditionalities, the most prominent was the removal of government subsidies on all social services. Our military strongman delighted Nigerians by refusing the loan, bragging that Nigeria would do it without borrowing. Thus began the era of step-wise official devaluation of the Naira and steep reduction of subvention to health services in real terms, but concealed by devaluation.

All public health institutions had to introduce user fees to survive. This became an impediment to the villagers who were just beginning to bring their health problems at earlier clinical stages. There was a big drop in hospital attendance and the status quo ante was more or less restored. We should always remember that, out there, there are great stories of miraculous cures by traditional healers, and it is not easy for anyone brought up in that culture to be sceptical.

The poor people first do the rounds among traditional healers where reception is warmer and payment more affordable because it can be in the form of some farm produce, on loan, or even free. The great confidence talks, shuffling a few human bones here and here, incantation to ancestors or the ritual eating of a sacrificial chicken cooked over a ritual fire have great healing powers on psychosomatic ailments, and believe me, they form the majority of the complaints out there. Such successes are extrapolated in circulating legends to all diseases, including organic ones like fractures and cancers, totally resistant to faith healing no matter how impressive the confidence performance might be. The result is that organic conditions land in hospital only when sufferers have sustained intolerable damage or are about to die.

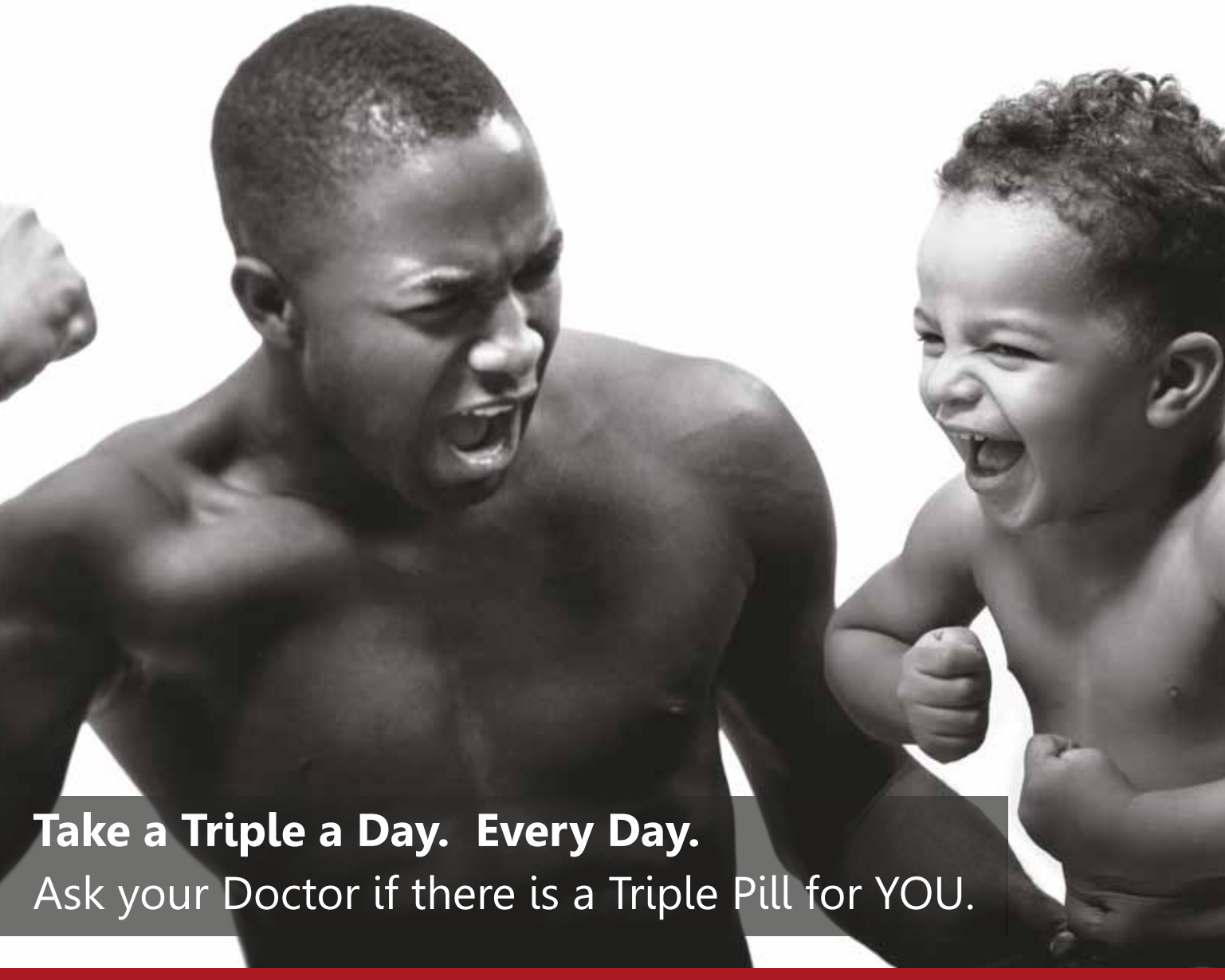
They may be turned away for inability to pay a deposit, and some die while looking for a way out. Others get the emergency treatment that saves their lives, but when they recover and no one turns up with the fees, they get detained for weeks or even months. Visit any ward and you will find quite a few prisoners of hospital fees that cannot go beyond the guards at the gates. The institutions themselves are severely underfunded and would grind to a halt within a few days if they did not get sufficient returns to purchase their working materials, and would not want to acquire a reputation that their determination to collect user fees can be easily overcome.

I had the pleasure of meeting international experts in health financing at a conference recently arranged by the Nigerian Health Watch. I was surprised to hear that the World Bank has done a complete about-turn on user fees for the poor and now regards them as unethical. It now accepts that universal coverage cannot be achieved without public subvention of the very poor. There were even suggestions that detaining anyone for inability to pay hospital fees constitutes violation of their human rights! This means that the governments of developing countries have lost their strongest external support for sidestepping their responsibility for funding the medical treatment for their poorest citizens. They must do so within or outside health insurance schemes.

Shima Gyoh has held many posts ranging from village doctor to DG of Nigeria's Federal Ministry of Health and Chair of the Medical and Dental Council of Nigeria.

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The African Region of the World Health Organization convenes in Njamena, Chad



Moeti's transformational agenda for WHO Afro needs proactive support from member states if it is to work, says Francis Omaswa

The 65th Regional Committee Meeting of the World Health Organization (WHO) Africa will meet at the end of this month in Ndjamena, Republic of Chad. The meeting is taking place later than usual partly due to security issues in the host country. I am glad that the Republic of Chad is able to host the meeting.

As we prepare to go to this meeting, it is my hope that we remember the routine that we have discussed previously on how delegations prepare for international meetings. It is a critical meeting for a number of reasons and a review of the draft agenda shows the importance of this committee.

It will be the first meeting under the leadership of the new Regional Director, Dr. Matshidiso Moeti. Dr Moeti has been working during her first year in office to develop 'The Transformation Agenda of the WHO Secretariat in the African Region 2015 - 2020', which will be put before Ministers for note and endorsement. According to Dr. Moeti, 'the Transformation Agenda marks a commitment to positive change. Its objective is to ensure that the WHO Secretariat in the African Region evolves into the primary leader in health development in the region, and a reliable and effective protector of Africa's health. The Transformation Agenda has four focus areas, namely: pro-results values, smart technical focus, responsive strategic operations, and effective communication and partnerships'. I hope that delegations will engage the Regional Director on this agenda and go back home committed to supporting Dr. Moeti in her noble cause for Africa.

There will be a discussion on lessons learnt from the West African Ebola outbreak which will provide an opportunity for delegates to appreciate the need for each and every country to have plans for preparedness and core capabilities to respond to infectious disease outbreak ideally working with affected communities to arrest the epidemics at the level where they first occur, thus stopping them from becoming global health risks. Compliance with the International Health Regulations (2005) should also fit into this agenda as most African countries are not compliant with reporting requirements. Another linked agenda item is stocktaking of the performance of The African Public Health Emergency Fund (APHEF), which is not performing well at all as very few member states are making contributions to it. The Progress report on the establishment of the African Centre for Disease Control and Prevention (CDC) is closely related, and I hope it will be possible for Health Ministers to speak with one voice at the African Union and the WHO Regional Committee so that an effective collaborative and non-competitive relationship between WHO and the African CDC will be built, taking full advantage of existing capacities in the African region.

This meeting takes place soon after the adoption of the Sustainable Development Goals (SDGs) and the transition from the MDGs, and is being discussed under the heading of, 'Progress on health-related Millennium Development Goals and the post-2015 health development agenda'. SDG 3 on health states, 'Ensure healthy lives and promote wellbeing for all at all ages'. How African countries will be assessed by the United Nations will be against performance on delivering on the SDGs. Development partners will also move to align their resources to the SDGs. It will therefore be useful for African countries to understand the SDGs as early as possible and start to work within their framework as this is the new global compact on our future under the banner, 'Transforming Our World - the 2030 Agenda for Sustainable Development'.

There are several other important agenda topics, such as the new Global Health Workforce Strategy, where it has been noted that a significant number of African countries are experiencing declining population to health worker ratios over the last ten years, despite a vigorous campaign on the matter. Working conditions for health workers remain a challenge and many have succumbed to infectious diseases acquired in the course of duty such as Ebola, hepatitis and HIV. There is also an agenda on health research which deserves attention and has important implications for health systems strengthening.

There are also many information sharing sessions containing good news such as the progress with polio eradication, health promotion, and women's health.

Francis Omaswa, CEO, African Centre for Global Health and Social Transformation (based from Kampala); Founding Executive Director of the Global Health Workforce Alliance.

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Maternal and Newborn Health Innovations Project launched in Kenya

UNICEF and The Philips Foundation, together with Concern Worldwide, and Maker and Gearbox, have launched the Maternal and Newborn Health Innovations Project, to help save lives and improve the health of pregnant women and children in Kenya.

Under the leadership of the Government of Kenya and the Project's Steering Committee at the Ministry of Health, UNICEF and The Philips Foundation will facilitate the development of innovative health technology and solutions in the field of maternal, newborn and child health.

This investment is in keeping with the Government of Kenya's commitment to investing in innovative, home-grown solutions.

Kenya has reduced under-five child deaths per 1000 lives from 90 in 2003 to 52 in 2014, but this still falls below the Millennium Development Goal 4 target of 33 by the end of 2015. Neonatal mortality is also very high at 22 deaths per 1000 live births.

By 2018, UNICEF and The Philips Foundation, together with partner organisations and local innovation hubs, and with guidance from the Government of Kenya, aim to develop and scale-up innovative, low-cost and locally designed healthcare devices.

'For 1 million babies worldwide every year, their day of birth is also their day of death,' said Sharad Sapra, UNICEF Director of the UNICEF Global Innovation Centre. 'But with strengthened health systems and innovative solutions for both mothers and children, the chance for survival is greatly increased.'

The Maternal and Newborn Health Innovations Project is financed by The Philips Foundation and uses the local expertise of Philips Research Africa in Nairobi to mentor social entrepreneurs and facilitate the transfer of healthcare technology know-how in Kenya.

'At The Philips Foundation, it is our belief that programmes that combine innovation, partnerships and empowering people will make a lasting and meaningful difference in communities,' said Katy Hartley, Head of The Philips Foundation. 'In the case of the Maternal and Newborn Health Innovations Project, we are doing just that, as Royal Philips can offer expertise and support from its Philips Research Africa, together with UNICEF and our implementation partners, to enable social entrepreneurs to improve health outcomes for their own communities.'

Rift Valley Fever kills four in Mauritania

The Rift Valley Fever (FVR) has claimed four lives in Mauritania, the Mauritanian Health Minister, Ould Ahmedou Ould Hademine Jelvoune said.

According to the minister, who was speaking to TV channel Al-Mouritaniye, the first case was diagnosed on 14th September 2015.

A second case occurred on 24th September followed by several others on 2nd October.

Jelvoune explained that it is not the same fever that has been widely diagnosed in recent months among Nouakchott residents.

People with FVR are usually treated before reaching the haemorrhagic stage and the death rate among them is between 1%-3%, he added.



Photo from http://phil.cdc.gov/

In most cases, humans are infected with FVR after direct or indirect contact with the blood or organs of infected animals.

The virus can be transmitted when handling infected animal tissues or during foetus or carcass disposal, according to the World Health Organization.

Salmonella unmasked as major killer of young children in Africa



Photo credit: Rocky Mountain Laboratories, NIAID, NIH

Invasive Salmonella infections in sub-Saharan Africa are a major cause of child illness and deaths, a new body of research into this usually overlooked infectious disease has revealed.

In the West, Salmonella is commonly thought of as a bacterium responsible for relatively benign cases of food poisoning. However, a supplement to the leading infectious diseases journal *Clinical Infectious Diseases* now exposes the unacceptable toll of sickness and death caused by invasive Salmonella infections in sub-Saharan Africa.

The supplement, sponsored by New Zealand's University of Otago and supported by a grant from the Bill & Melinda Gates Foundation, is a key output of a project to better understand the disease burden of this major cause of child death in sub-Saharan Africa.

Guest edited by Professor John Crump, Co-Director of the University's Centre for International Health, and by Professor Robert Heyderman, Professor of Infectious Diseases and International Health, at University College London, the supplement emerged from a consensus meeting of experts held in Malawi last year, supported by the Wellcome Trust and Bill & Melinda Gates Foundation.

The supplement includes 19 scientific papers that describe the toll of invasive Salmonella infections in Burkina Faso, Ethiopia, Gambia, Ghana, Guinea-Bissau, Madagascar, Mali, Nigeria, Kenya, Democratic Republic of Congo, Malawi, Mozambique, Senegal, South Africa, Sudan, and Tanzania.

It also includes papers on the application of genetic fingerprinting and mathematical modelling to understand disease sources and modes of transmission, as well as vaccines and other prevention measures.

Experts want medical dosage in local dialects



Kenya and other African countries should adopt cultural approaches to combating diseases, health experts have said.

Speaking at the Fifth Africa Governance, Leadership and Management Convention in Kwale County, the experts called for the translation of medical prescription and medicine dosage to native language to allow rural residents to understand them.

'For community-based health systems to be a success, the private sector and government should come together and translate medical information so that even the prescription is written in native languages,' said Dr. Nicholas Letting, the Vice Chancellor of Management University of Africa.

Martine Kappel, the founder of True North Leadership, a governance consultancy, said the government should facilitate traditional medication. 'Not all African tradition healers are bad. There are African medicines that assist in the fight against some diseases that should be encouraged,' said Kappel.

The experts said Kenya and most other African countries have not adopted a community-based health services approach to combat outbreaks of infectious diseases and other epidemics like cholera and Ebola.

For Africa to succeed in the fight against common diseases, the Chancellor of Moi University, Prof Mariam Were said, it should roll-out community-based health approach.

'Kenya is still at a very high-risk if an infectious disease breaks out. The government started to implement the community-based health approach in 2008, but it did that to only those areas that had cholera outbreak,' she said.

Ethiopia and Ghana were cited as the countries that have successfully implemented community health approach. 'Ghana successfully dealt with the Ebola threat because its health system is perfect. It was able to deal with it because of the vibrant community-based health system,' said Were.

Scientists mark 'stunning success' of vaccine in virtually ridding Africa of meningitis A

Five years after the introduction of an affordable conjugate meningitis A vaccine, immunisation has led to the control and near elimination of the deadly disease in the African 'meningitis belt'.

The findings are part of a special collection of 29 articles in the journal *Clinical Infectious Diseases*, with guest editors from Public Health England and the former Meningitis Vaccine Project, a partnership between the World Health Organization (WHO) and the international health non-profit PATH, about the steps taken for the development, introduction, and evaluation of the PsA-TT conjugate meningitis A vaccine for Africa, better known as MenAfriVac®.

But scientists are now warning that unless countries within the belt incorporate the meningitis A vaccine in routine immunisation schedules for infants, there is a risk that the disease could rebound in 15 years' time.

'We have nearly eliminated meningitis A epidemics from Africa, but the fact is the job is not yet done,' said Dr. Jean-Marie Okwo-Bele, Director of Immunisation, Vaccines and Biologicals at WHO.

The vaccine was developed in response to a plea for help from ministers of health in sub-Saharan Africa after an outbreak of meningitis A in 1996 that infected over 250 000 people and killed over 25 000 in just a few months. The vaccine costs less than US$0.50 a dose.

When scientists followed up with 900 people aged 2 through to 29 years from Senegal, Mali, and The Gambia who were vaccinated with MenAfriVac®, they found that 90% of individuals still had protective antibodies in their system five years later. Study authors said this is a good predictor of even longer-term protection that they will continue to track.

'We need to ensure that we finish the job with meningitis A and apply the lessons learned to the next generation of meningitis vaccines for Africa,' said Dr. Marc LaForce, who formerly led development of the meningitis A vaccine for PATH and is now with Serum Institute of India.

Facebook developing satellite internet for Africa

Facebook and French satellite operator Eutelsat wants to launch an internet-satellite that could boost internet connectivity in more than 14 African countries.

Easier and more reliable access to the internet could offer substantial benefits to social, educational and healthcare ideals of the National Development Plan.

The Facebook-financed satellite, named Amos-6, would be able to offer faster and more reliable internet access to isolated areas in Africa.

'Facebook has been exploring ways to use aircraft and satellites to beam internet access down into communities from the sky,' Mark Zuckerberg wrote. 'To connect people living in remote regions, traditional connectivity infrastructure is often difficult and inefficient, so we need to invent new technologies.'

The satellite project is part of Facebook's Internet.org non-profit initiative that aims to bring free and reliable internet access to the two-thirds of the world that have been unable to receive it.

Sub-Saharan Africa's current level of broadband connectivity is the lowest in the world, according to the United Nations' 2014 State of Broadband report. It reaches less than 2% of the populations in countries such as Guinea, Somalia, Burundi, and Eritrea. The internet remains a novelty and not so much the vital communications tool needed to push African development and innovation forward.

Governments will be able to use the surge in access to bring better services to people in rural areas.

Toby Shapshak, a technology trends expert, said that satellites offered the best option for African internet access. With the Facebook investment, the idea of bringing fast, reliable and cost-effective internet to Africa is slowly becoming a reality.

Korle Bu gets modern eye treatment centre

The Korle Bu Teaching Hospital Department of Ophthalmology is the beneficiary of a modern specialist eye centre, which will also serve as a West Africa regional surgical training facility.

The new stand-alone centre, named 'Lions International Eye Centre,' was made possible through a fundraising campaign, which raised over $3 million, led by Moorfields Eye Hospital (MEH) of the United Kingdom and the Lions Club International (LCI).

Commenting on the new eye centre, Dr. Steven Akafo, a Consultant Ophthalmologist at Korle Bu Teaching Hospital, said: 'My vision is that no eye patient should have to leave Ghana for treatment.'

The centre has two theatres, three wards, a minor treatment room, a 12-bed bay, offices, and consultants rooms. There is also an optical shop that offers optometry services and dispenses spectacles.

A Past District Governor of LCI, Mrs Gloria Lassey, said the LCI Foundation operated a 'Sightfirst' programme which funds the activities of Lions, non-governmental organisations, government agencies, and others to fight the major causes of preventable and reversible blindness. She said that the foundation also provided services for people who were blind or visually impaired by supporting eye healthcare delivery systems, training and infrastructure development, particularly in underserved communities throughout the world.



Photo credit: Alaine Kathryn Knipes; Parasitic Disease Branch (DPDx); Division of Parasitic Diseases and Malaria

Twelve doctors have benefitted from four surgical training courses, which included glaucoma, small incision cataract surgery, eyelid surgery, and a special course for training of trainers.

'With the development of this new integrated training and treatment centre, West Africa will be a vanguard for sub-speciality training in ophthalmology, which is very exciting,' stated Dr. Murdoch.

Dr. Folasade Akinsola, Past Chairman, Faculty of Ophthalmology, West African College of Surgeons, also noted that, 'developing sub-specialist surgical skills will ensure comprehensive and quality eye health services are available across West Africa, reducing avoidable blindness in line with Vision 2020 objectives.'

Ethiopia to strengthen outbreak preparedness partnering with US CDC

The US Centers for Disease Control and Prevention (CDC), has awarded funds to the Ethiopian Public Health Institute (EPHI), African Society for Laboratory Medicine (ASLM), and American Society for Microbiology (ASM) to support the Global Health Security Agenda (GHSA).

This investment will strengthen preparedness efforts to rapidly detect and respond to infectious diseases threats, such as Ebola and other emerging diseases. Additionally, the activities will advance progress toward compliance with the International Health Regulations, a World Health Organization effort to improve emergency preparedness and response capabilities in all countries.

These partnerships illustrate commitment to GHSA in Ethiopia and the acceleration of progress toward a country and a world safe and secure from infectious disease threats. 'The recently released Health Sector Transformation Plan underscores how Ethiopia's strategy aligns with GHSA, which is a strong indication that EPHI can make significant strides towards preparedness,' said CDC Ethiopia Country Director Jeffrey Hanson.

GHSA promotes global health security as a national priority through targeted capacity building activities, such as improving laboratory systems, strengthening surveillance systems, expanding workforce development, and improving emergency management.

The US has also committed to helping at least 30 countries achieve all of capacity building targets of GHSA by the end of 2019, and is investing resources and technical assistance to attain this goal.

HIV vaccine could be a reality soon, say researchers



Photo credit: Jon Rawlinson. https://www.flickr.com/photos/london/7146233 1

A South African research team has published a study that has significant implications for the development of an HIV vaccine, although how far away the practical application is, remains difficult to measure.

Researchers from the University of the Witwatersrand (Wits), the Centre for the Aids Programme of Research in South Africa, and the University of Cape Town (UCT) released a statement confirming that their team, which included a PhD candidate at Wits, had published a seminal study that could be a decisive step towards a working vaccine.

The study, in a nutshell, focuses on a process that could drive the production of 'broadly neutralising' antibodies that could fight and destroy various mutations of the human immunodeficiency virus (HIV).

'The development of a vaccine remains the best possibility for ending the HIV pandemic,' Wits's senior communications officer, Kemantha Govender, said. 'However, the researchers say that a major challenge has been the inability to stimulate broadly neutralising antibodies that are able to deal with the enormous variability of HIV.'

The PhD candidate, Jinal Bhiman, was the lead author of the study, which was published in the *Nature Medicine* journal.

The researchers previously discovered a vulnerable spot on the outer shell of the HIV cell, which enabled the production of the powerful antibodies. During their long-term follow-ups with the patients participating in their study, they found that a glycan, a form of sugar, in a particular position on the protein coat covering the virus cell was a weak spot that could be attacked by the neutralising antibodies.

'We need to keep looking for a vaccine,' Goemaere said. 'It is difficult to predict how long it will take. It is very promising in the lab, but we still need to prove that for humans it can make a difference. It is just going to take time. We cannot bring down this epidemic just by treating all the cases; we need some preventive tools. In the long-term, we do need a vaccine.'

Kenya first country to launch Novartis Access

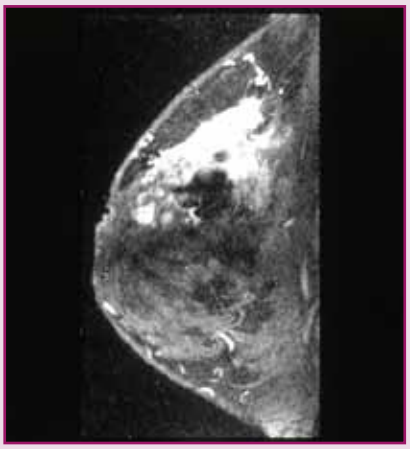


Photo credit: This image was released by the National Cancer Institute, an agency part of the National Institutes of Health, with the ID 2703

Novartis announced the launch of Novartis Access in Kenya, the first country to benefit from a portfolio of 15 affordable medicines to treat cardiovascular diseases, diabetes, respiratory illnesses, and breast cancer.

The Novartis portfolio is being offered to the Kenyan government, non-governmental organisations, and other public-sector healthcare providers for US$1 per treatment, per month.

'Novartis and Kenya have a relationship of more than 40 years, so I am delighted that Kenyan patients will be the first to benefit from Novartis Access,' said Joerg Reinhardt, Chairman of the Board of Novartis. 'The successful implementation of the programme in Kenya will be essential to guide the expansion of Novartis Access to other countries in the future.'

Some 28 million people die from chronic diseases in low- and middle-income countries each year, representing 75% of such deaths globally. In Kenya, non-communicable diseases (NCDs) account for 27% of deaths, or almost 100 000 people per year. By 2030, NCDs are expected to contribute to more than 60% of the total national mortality.

'I am excited by the proactive steps being taken by our government and Novartis in the fight against cancer and other chronic diseases,' said H.E. Margaret Kenyatta, First Lady of the Republic of Kenya. 'Novartis Access complements the advocacy campaign I have been undertaking together with other African First Ladies to expand access to prevention and treatment for people with chronic diseases.'

To find out more about Novartis Access, visit www.novartisaccess.com.

President of Liberia keynotes gala for Global Health to support infectious disease research

President Ellen Johnson Sirleaf of Liberia delivered the keynote address at the 11th Annual Gala for Global Health, as the Centre for Infectious Disease Research raised hundreds of thousands of dollars to support its pioneering research to find vaccines, drugs and diagnostics for the world's deadliest infectious diseases.

More than 700 guests attended the event in Bellevue to support the Centre and see President Sirleaf speak about the challenges of leading a country devastated by Ebola and other infectious diseases. Paul G. Allen, philanthropist and founder and chairman of Vulcan Inc., was also in attendance to receive the Centre's 'Champion for Global Health Award'.

'It was a tremendous privilege to host President Sirleaf and Mr Allen at our gala,' said Alan Aderem, PhD, President and Director of the Centre for Infectious Disease Research. 'We are incredibly thankful to the hundreds of people who came to see these inspiring individuals speak and support our critical mission of developing vaccines, drugs and diagnostics to help save the lives of the millions of people who die from infectious diseases every year.'

At the conclusion of President Sirleaf's speech, Lisa Cohen, Executive Director of the Washington Global Health Alliance, moderated a question and answer session with President Sirleaf, Dr. Aderem, and Trevor Mundel, PhD, President of the Global Health Division of the Bill and Melinda Gates Foundation.

As well as being awarded the 'Champion for Global Health Award', Mr Allen has also been a key leader in the fight against Ebola. As the largest private donor, he pledged $100 million to the effort and established The Paul G. Allen Ebola Programme, the only programme of its kind focused on ending Ebola in West Africa.

'Thanks to the courage and incredible work of thousands of people in the global and West African health communities, the leadership of President Sirleaf and other elected officials, and the tireless efforts of organisations, including the Centre for Infectious Disease Research, we have made meaningful progress in the fight against Ebola and other infectious diseases,' said Mr Allen.

Stefan Kappe, PhD, Professor and Director of translational science at the Centre for Infectious Disease Research, also announced during the gala that the Centre is in the process of finalising a new partnership with Group Health to begin the next phase of clinical trials for a promising malaria vaccine candidate.

Ebola crisis spurs new WHO reform programme

The World Health Organization (WHO) chief said preparedness, awareness, and transparency are at the heart of the WHO reform process.

WHO Director General Margaret Chan said many lessons have been learned from the Ebola epidemic in West Africa and these will be incorporated in the reform process that is underway.

She said being prepared is decisive in fighting any epidemic or pandemic of such magnitude. She said that involves shoring up and strengthening the resilience of fragile health systems in Africa and elsewhere in the world. 'In the past, when we talk about a health system, the tendency is to talk about clinical care, curative care. And now we should integrate the public health disease surveillance and laboratory testing as part of the health system capability,' she stated.

As part of the reform programme, Dr. Chan said WHO is building a global emergency health work force. She said trained foreign medical teams will be on standby, ready to respond rapidly to a disease outbreak or natural disaster in any country.

She said decisive leadership, awareness of the dangers posed by an epidemic and being transparent about these problems are critical in controlling an outbreak.

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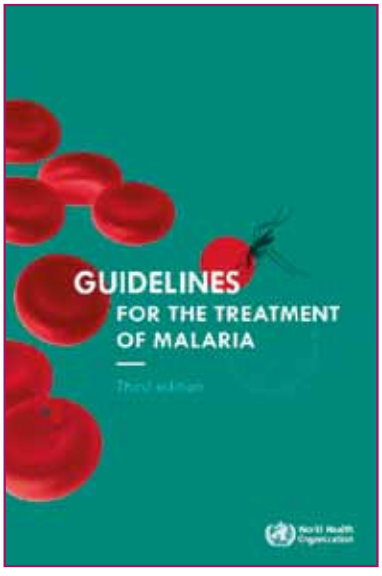
Plasmodium vivax 'returns' to Africa to threaten health

Whilst more benign than *P. falciparum* for instance, the reappearance of *P. vivax* is a concern as it is much more difficult to detect. Professor William Brieger reports

According to Weimin Liu and colleagues[1] reporting in the journal *Nature*, '*Plasmodium vivax* is the leading cause of human malaria in Asia and Latin America but is absent from most of central Africa due to the near fixation of a mutation that inhibits the expression of its receptor, the Duffy antigen, on human erythrocytes', it was thought to be rare in Africa. This perception arises because of the near absence through genetic mutation of 'the Duffy antigen receptor for chemokines (DARC) which is used by *P. vivax* merozoites to invade red blood cells'. Unfortunately, *P. vivax* is now being identified much more often in Africa.

Locations and origins

Liu et al propose that *P. vivax* actually began in Africa and they looked at wild-living apes in central Africa to find evidence of its origins. They found, 'widespread infection with diverse strains of *P. vivax* and harbor a distinct but related Plasmodium species provides new insight into the evolutionary history of human *P. vivax*, and potentially solves the paradox that a mutation conferring resistance to *P. vivax* occurs at high frequency in the very region where this parasite is absent'. They concluded that human *P. vivax* arose from within a Plasmodium species that infects chimpanzees and gorillas, which indicates an origin in Africa rather than, as previously assumed, in Asia. Regardless of the origins, *P. vivax* is staking claims in Africa today.



Coming back to infections in people, Mendes et al (2014)[2] demonstrated that, '*P. vivax* infections were found both in humans and mosquitoes' in Angola and Equatorial Guinea. This means that active transmission is occurring.

'Given the high prevalence of infection in mosquitoes', they speculated that 'this hypnozoite-forming species at liver stage may not be detected by the peripheral blood samples analysis'. In Ethiopia a serological study of school children by Ashton and co-workers found widespread seroprevalence of *P. vivax*.

In northern Angola among polymerase chain reaction-tested blood samples that contained plasmodium species, 1.1% were *P. vivax* alone.[3] In Huambo Province[4] in the middle of Angola, data from health information system laboratory data revealed that 15% of malaria cases detected were *P. vivax*. Clearly this parasite is present in Africa, but in varying degrees and needs to be monitored.

Once thought to be a more benign species, *P. vivax* is now seen for the dangers it brings in terms of morbidity and mortality in children, pregnant women and adults. Several major concerns include the fact that this species has a hibernating stage that makes sub-clinical, submicroscopic infection possible, thus thwarting detection and elimination efforts.[5]

The World Health Organization's (WHOs) malaria case management guidelines (2015)[6] note that, 'Of the species of Plasmodium that affect humans, only *P. vivax* and *P. ovale* form hypnozoites, which are dormant para-



William R Brieger is a Professor for the Department of International Health, the Johns Hopkins Bloomberg School of Public Health, and Senior Malaria Specialist, Jhpiego, an affiliate of the Johns Hopkins University.

site stages in the liver that cause relapses of infection weeks to years after the primary infection'. Special and more expensive rapid diagnostic tests (RDTs) are needed that detect both the more common *P. falciparum* as well as *P. vivax*. Hypnozoites have also assumed a new significance because they might, by facilitating ongoing transmission, be a threat to the goal of eliminating malaria globally according to Markus.[7]

Plasmodium vivax treatment

WHO explains that *P. vivax* is generally still sensitive to chloroquine, but resistance is increasing. The challenge in Africa where co-infection with *P. falciparum* is possible, chloroquine sensitivity is lacking and artemisinin-based combination therapy (ACTs) are required, although *P. vivax* is also sensitive to ACTs. WHO also notes that, 'In contrast to *P. falciparum*, asexual stages of *P. vivax* are also susceptible to primaquine'.

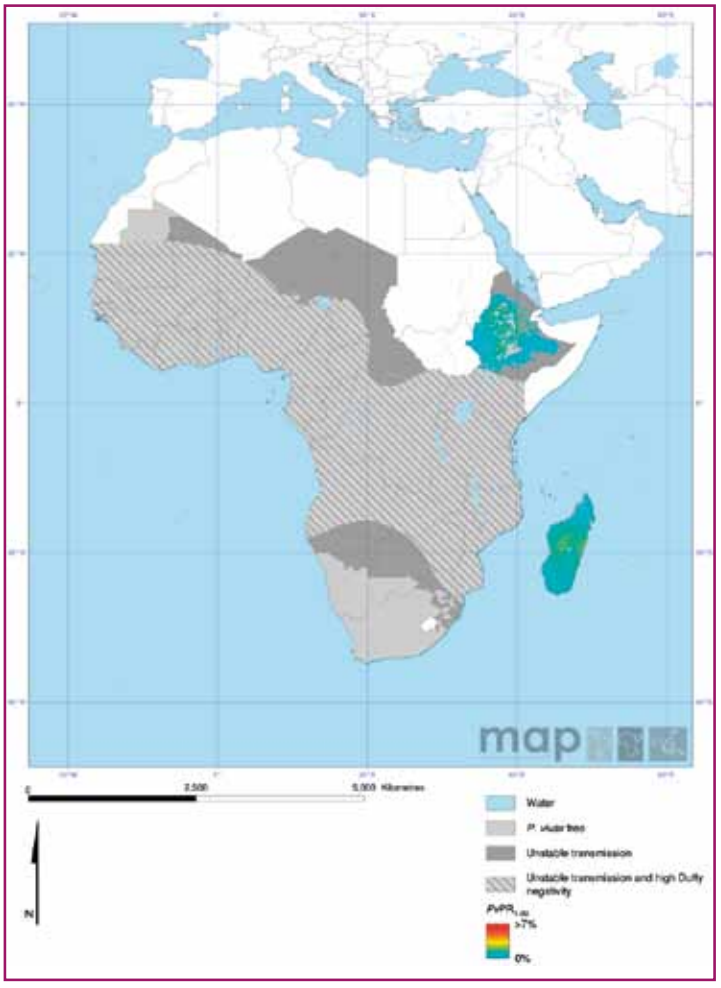
WHO addresses the issue of *P. vivax* relapse as follows: 'To prevent relapse, treat *P. vivax* malaria in children and adults (except pregnant women, infants aged < 6 months, women breastfeeding infants < 6 months, women breastfeeding older infants unless they are known not to be G6PD deficient and people with G6PD deficiency) with a 14-day course of primaquine in all transmission settings. This is a strong recommendation with high-quality evidence'.

WHO explains that a person with red cell G6PD activity < 30% of the normal mean has G6PD deficiency, and such person he will experience haemolysis after primaquine. We should again note that G6PD deficiency is an inherited sex-linked genetic disorder, which is associated with some protection against *P. falciparum* and thus less common in Africa. Furthermore WHO advises that, 'The severity of haemolytic anaemia depends on the dose of primaquine and on the variant of the G6PD enzyme. Fortunately, primaquine is eliminated rapidly so haemolysis is self-limiting once the drug is stopped. Primaquine is contraindicated in pregnant women and in lactating women (unless the infant is known not to be G6PD deficient'.

Again, WHO observes that even in areas where the condition and *P. vivax* are common, 'Screening for G6PD deficiency is not widely available outside hospitals, but rapid screening tests that can be used at points of care have recently become commercially available'. Such tests are indeed rarely available in Africa and would increase cost and delay in treatment.

Surveillance and planning

In 2012 Shanks[8] wrote that, 'It is likely to be some years before anyone will consider relapsing malaria a major problem in Africa, but it will be important in terms of elimination programmes when and if the burden of falciparum malaria is reduced to levels where non-falciparum species make up most of the malaria infections'. Even so, he does not suggest ignoring the problem but recommends better reporting and surveillance of non-falciparum species



Spatial distribution of Plasmodium vivax malaria endemicity map in 2010 in WHO AFRO Region. http://www.map.ox.ac.uk/browse-resources/endemicity/Pv_mean/afro/

in sub-Saharan Africa as an important step to amass data for future intervention.

Surveillance brings us to the point of looking at what detection methods we have for *P. vivax* in Africa, especially under frontline clinic and field conditions where rapid responses will be necessary as areas and countries move toward malaria elimination. The Centers for Disease Control and Prevention (CDC)[9] explains that there are two types of RDTs for malaria, some for *P. falciparum* only, and one that detects *P. falciparum* and others that determine the presence of *P. falciparum* and other species. CDC advises that, 'The tests must also be affordable to national malaria programmes. The costs of the tests have fallen in the last few years; even so, many malaria control programmes find that procuring the large numbers of test kits needed to ensure universal diagnosis is a considerable expense'. The typical RDT used in Africa to detect *P. falciparum* costs less that US$0.50 (excluding additional factors such as shipping, storage, staff, etc.).[10]

That said the tests with the ability to detect antigens from two malaria species are more expensive. There are many RDT products. Out of 128 unique products tested by Foundation for Innovative New Diagnostics (FIND), 83 detect and differentiate *P. falciparum*

from non-*P. falciparum* malaria (either pan-specific or species-specific (Pv, Pvom).[11]

Donors and African endemic countries may be reluctant to pay the additional price for the dual capability tests, but as *P. falciparum* declines and *P. vivax* becomes more evident, they will need to rethink their positions in order to detect all malaria cases and eliminate the disease from their territories.

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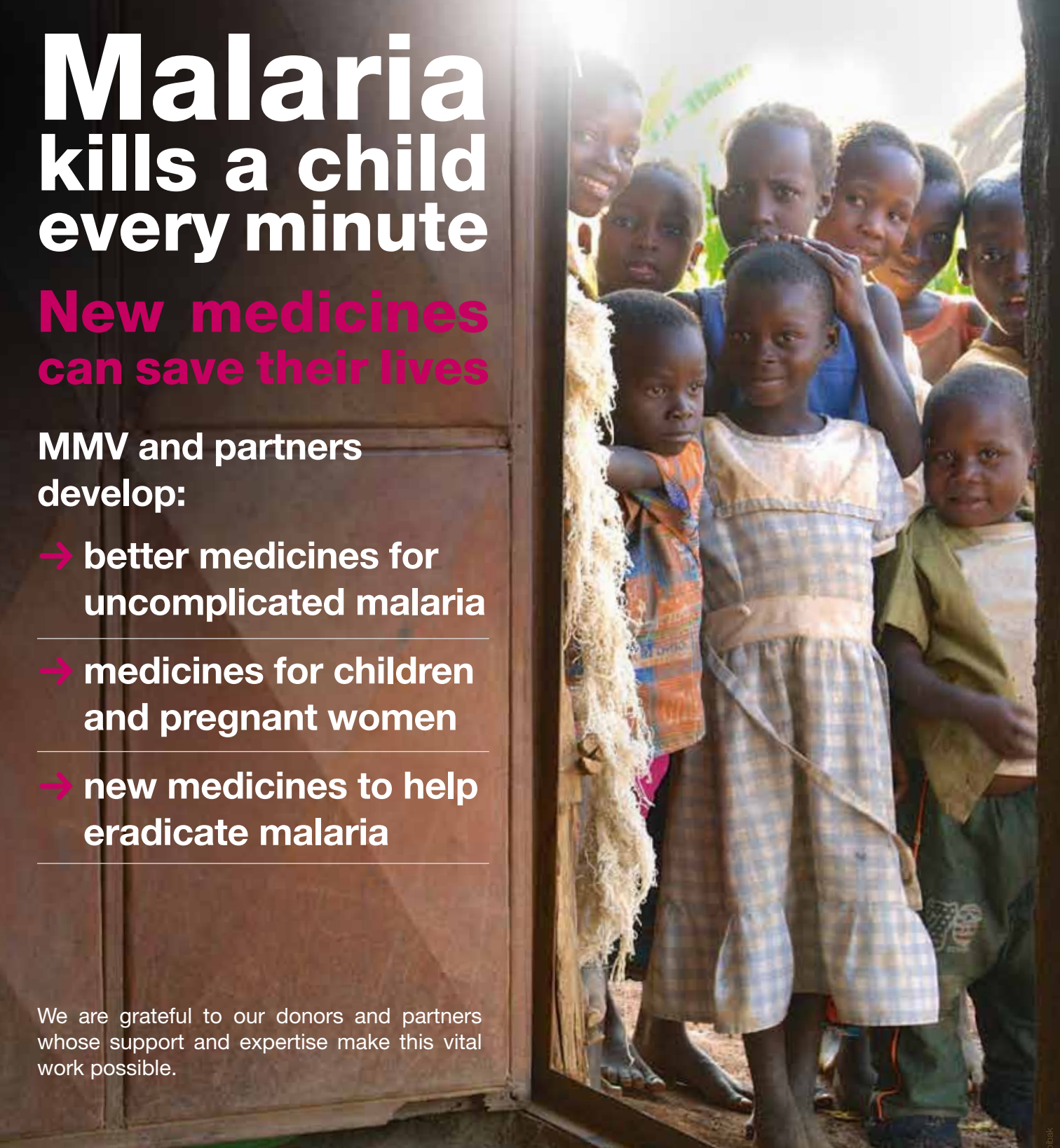


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Supporting adherence to new malaria treatment with user-friendly materials

Medicines for Malaria Venture's Maud Majeres Lugand explains the importance of designing training materials and packaging to support the correct administration of medicines

The potential impact of any new antimalarial can only be fully realised if it is used correctly. To support this, medicines must be accompanied by appropriate materials to help facilitate correct administration and adherence to the dosing schedule. Clear and user-friendly communication materials are thus critical to improve treatment outcomes.

There are a number of reasons why patients may not adhere to treatment or complete the full course of medication. A study that examined adherence to an artemisinin-based combination therapy found that many patients stopped their medication once they felt better, or failed to complete the course because there were too many tablets.[1] Others wanted to save some of the tablets for future episodes of malaria,[1] as in many regions, patients have to travel a long way to their first point of care.

> "By listening to the voices of patients and health workers who use medicines in the field, we improved our understanding of the '*human factors*' that can increase the impact of correctly used drugs - and we adapt our materials accordingly."
>
> *George Jagoe, Executive Vice President - Access & Product Management, MMV*

In addition, adherence to the dosing schedule may be negatively impacted when patients or caregivers struggle to understand dosing instructions.[2] This can be particularly problematic in populations with low levels of literacy. Providing simple patient information and pictograms has been shown to improve adherence.[3,4]

In collaboration with in-country partners, Medicines for Malaria Venture (MMV) has invested significant resources in designing and testing packaging and visual aids to help ensure that the drug administration process is clearly understood by both patients and health workers.

Listen and learn: interacting with users to develop the right materials

By field testing communication materials, comprehension can be evaluated in a 'real-life context'. The primary challenge in field testing is to incorporate end-user comments in real time, and adapt materials until they are readily understood by a majority of users.

Dosing instructions are often given verbally, with the patient or caregiver having only the information provided on the packaging as a reminder. Pictorial guides on packaging have been shown to increase understanding about the timing of doses and the importance of completing a course of therapy.[5] The purpose of these visual aids is to provide clear, simple, step-by-step instructions on what actions to take. To be successful, these resources need to meet a number of criteria. They must:

- Be clearly understood by end users
- Present a message that is relevant to the user
- Convey a message that convinces the user to undertake the desired behaviour
- Be socially and culturally acceptable.

To develop packaging and visual aids that meet these criteria, MMV field tests the early versions of the materials with end users in endemic countries. A key feature of this approach is the iterative process. The 'repeat factor' is important, as gaining feedback from different groups of respondents expands the range of perspectives and helps to achieve a balanced view. At each stage, the designer and researchers redesign the materials in response to the comments received. Because the designer is actually present in the field, talking with the end-users, they are able to redraw materials 'on the spot', and gain immediate feedback on these modifications. This innovative approach results in the materials evolving during the field work until they effectively communicate to the majority of likely end-users.

Arriving at this point in the cycle is rewarding, as the materials have not just been designed for end users, but with them.

Case study: field testing the Pyramax® dosing chart – less is best

Most antimalarials come in tablets of different strengths or in age/weight band specific packs with different numbers of tablets. This approach complicates stock management, forecasting, ordering and shipping. For example, a health centre may find itself with too many adult packets and too few child packets.

To avoid these problems, Pyramax®, the fixed-dose combination of pyronaridine and artesunate co-developed by MMV and Shin Poong Pharmaceutical, is dispensed in blister strips of three tablets of the same strength. Rising with body weight, the daily dose is 1, 2, 3, or 4 tablets, to be taken for 3 days.

To facilitate correct dispensing particularly at the

Maud Majeres Lugand is a Project Officer, Access and Product Management at Medicines for Malaria Venture

community level, user-friendly packaging with visual instructions was particularly important.

The field testing took place in Cambodia, India, Kenya and Senegal and involved 468 interviews with doctors, nurses, community health workers, caregivers and patients.

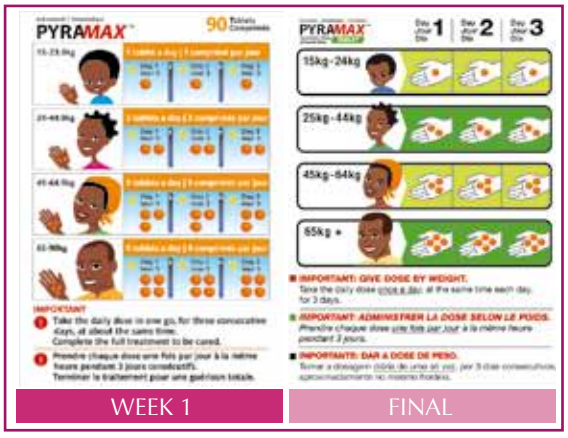


Figure 1. Evolution of the Pyramax® dosing chart

Two key pieces of information that the *Pyramax* dosing chart (Figure 1) needed to convey were:

1. The age-group for each weight-band dosing category (as *Pyramax* does not come in age-specific packs).
2. The dose is given once a day (not twice a day, as is well known for artemether-lumefantrine).

Results of the field testing showed that the patient illustrations helped the drug dispenser administer the correct dose. The cartoons were considered 'friendly' by interviewees, who thought they were an appropriate way to distinguish between the different age groups. The 'once a day' message needed more refinement. The sun and moon symbols were removed as too many people interpreted this as one dose in the morning and one in the evening. To emphasise taking the tablets in one go, the dose was shown in the palm of the hand (see Figure 1). This helped to clarify the message for end users. Simple text with a clean uncluttered design was most understandable.

Making the best use of primary packaging: the example of SPAQ-CO™ and Eurartesim®

Very often patient/caregivers receive only the blister pack accompanied by oral instructions for the administration of the treatment. The primary packaging thus provides a prime opportunity to reinforce key messages regarding the administration and dosage of medicines with the end user.

Given the limited space on an antimalarial drug package, the messages have to be very clear and concise. By testing different packaging designs with end users, MMV has helped to generate innovative packaging that facilitates correct dosing and adherence to treatment whilst also meeting the World Health Organization (WHO) requirements on packaging antimalarial medicines.[5]

In developing user-friendly packaging, we are working to accommodate competing requirements: communicating a large amount of information on a restricted space, and keeping packaging costs as low as possible. Simple, clear design is crucial to convey this information as can be seen below (Figures 2 and 3) with the blisters for SPAQ-CO™ (a co-blistered combination of sulfadoxine-pyrimethamine and amodiaquine recommended by

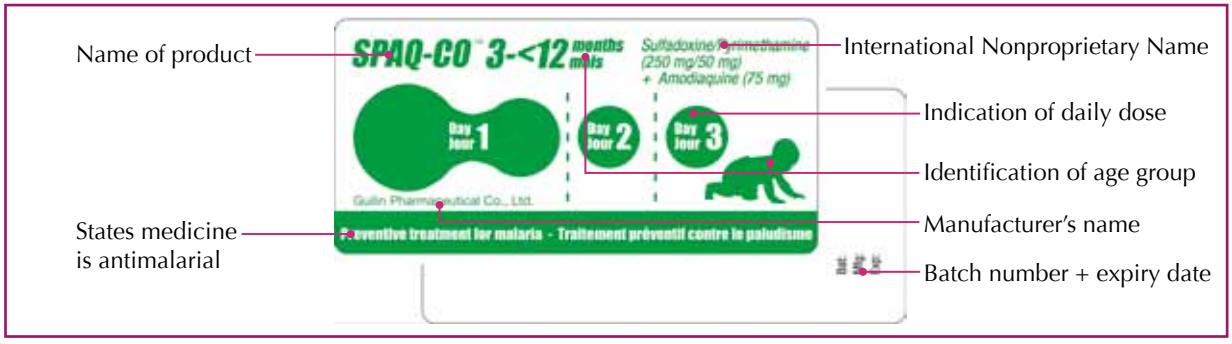


Figure 2. SPAQ-CO™ blister pack



Figure 3. Eurartesim® Cambodia packs and dosing chart

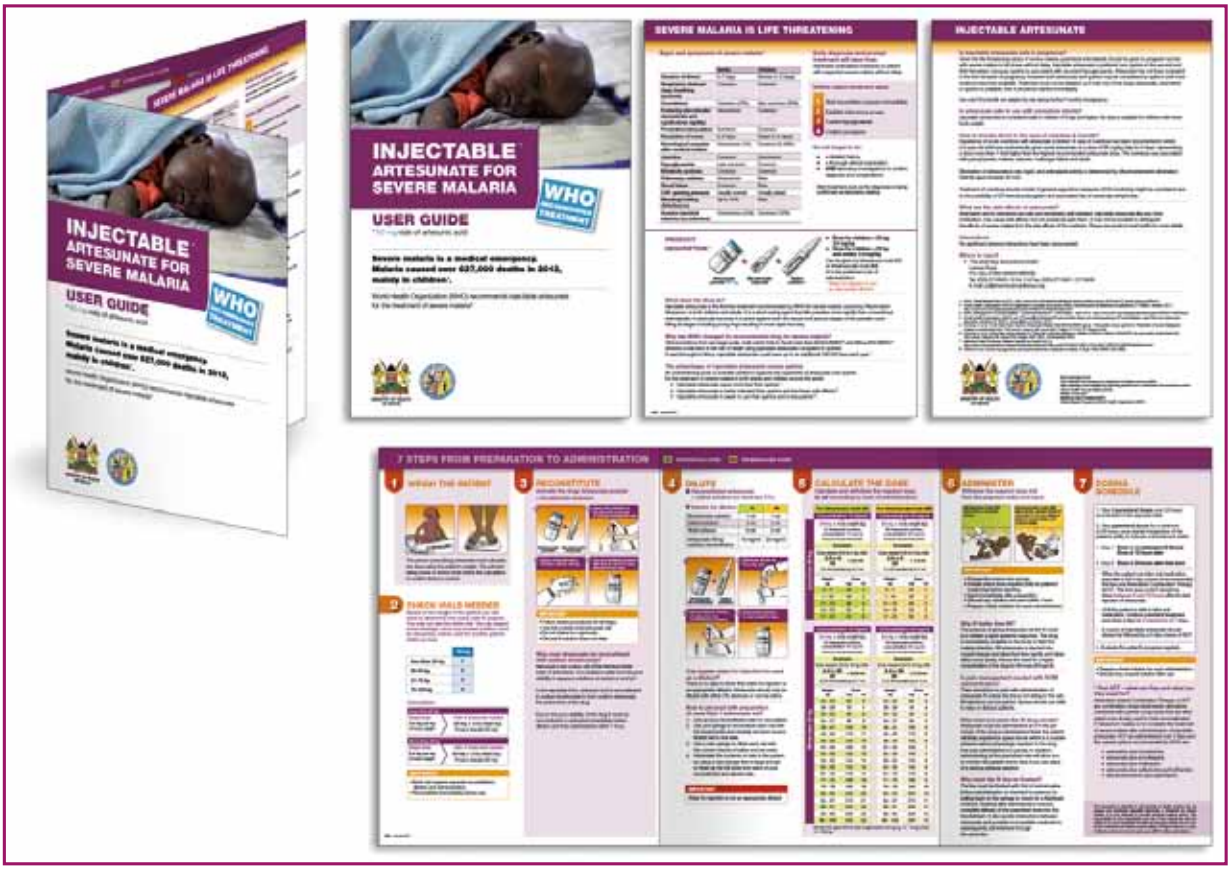


Figure 4. Injectable artesunate user guide from the toolkit

WHO for seasonal malaria chemoprevention, SMC) and Eurartesim® (a fixed-dose combination of dihydroartemisinin-piperaquine, developed by Sigma-Tau and MMV for uncomplicated malaria).

Working in partnership to share best practice

In addition to our work developing user-friendly packaging, MMV has worked closely with a variety of partners to create toolkits to support countries implementing SMC, and to help health workers correctly prepare and administer injectable artesunate for the treatment of severe malaria (see Figure 4). All these materials are available on the MMV website (www.mmv.org/access/tool-kits).

MMV's job aid for injectable artesunate has been widely adopted by 11 countries, including Cameroon, Kenya, Malawi, Nigeria, Uganda, South Africa and Zambia. Similarly, the launch of the SMC toolkit across the Sahel sub-region of West Africa has been supported by RBM's West Africa Regional Network (WARN) and is listed on the WHO malaria website as a useful resource.[6]

The knowledge we have gained extends beyond malaria. For example, we recently helped PATH develop packaging for a new dispersible tablet form of amoxicillin.

Working on these projects has given MMV considerable experience in designing and evaluating training materials for use in developing countries, and we are keen to share this experience. Through partnership and collaboration, the MMV Access and Product Management team will continue to work towards maximizing treatment outcomes by producing user-friendly materials to support new medicines.

> "The Injectable Artesunate visual aids are a very good intiative. They are very important as reference materials for healthcare workers. They really assist by providing information on administration including reconstitution and dosing of Inj. AS. Trainings on administration of Inj. AS would have been very difficult and time consuming without them."
>
> *Dr. Chalwe, Maina Soko Military Hospital, Lusaka - National Trainer (NMCC) - Administration of Inj. AS.*

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Diabetes and the gastrointestinal tract

Ian Forgacs
Omair Raja

Abstract
The range of gastrointestinal complications of diabetes extends from the mouth to the anus. In some cases the resulting conditions are familiar — such as gastro-oesophageal reflux and constipation — and the relevance of the diabetes is little more than that these conditions are seen more frequently in diabetic patients than in the general population. Indeed, the range of treatments and their effectiveness are the same in both groups irrespective of the presence of diabetes. But there are two unusual gastrointestinal complications that are peculiar to diabetes: gastroparesis and diabetic diarrhoea. The management of patients with these problems can be extremely challenging; apart from the sheer unpleasantness of chronic vomiting and diarrhoea to the point of incontinence, fluid depletion and loss of diabetic control may necessitate hospital admission. Both vomiting and diarrhoea can be intractable, and the disappointing response of both conditions to the existing range of treatments is often frustrating for patient and physician. Much of the difficulty stems from the fact that their aetiology is poorly understood. The skills involved in looking after such patients extend far beyond the prescribing manual.

Keywords Botulinum toxin; candidiasis; constipation; diabetes mellitus; diabetic diarrhoea; electrical gastric stimulation; gastro-oesophageal reflux; gastroparesis; serotonin antagonists

What's new?

- Rigorous attention to diet and judicious use of prokinetic drugs remain the cornerstone of treatment for most patients with gastroparesis
- Botulinum toxin injection to the pylorus is no longer recommended in refractory gastroparesis
- Electrical gastric stimulation ('gastric pacing') may rapidly improve symptoms in severe otherwise unresponsive gastroparesis
- Treating diabetic diarrhoea remains challenging but serotonin receptors and ghrelin receptors appear promising targets for future therapeutic intervention

Introduction

Although the gastrointestinal complications of diabetes mellitus (Figure 1) are clearly not as life threatening as those that affect some other systems, their consequences for a patient's quality of life can be profound. It is naïve to conclude that most of the more serious gastrointestinal complications of diabetes are simply a result of autonomic neuropathy. The correlation between severity of symptoms and degree of autonomic dysfunction is often poor. The control of the enteric nervous system is complex and the neurohumoral interactions extend beyond the sympathetic–parasympathetic system. A rational approach to diagnosis and therapy of the disturbances of the gut in diabetes would require much more understanding of its neurophysiology than has yet been revealed. Treatment is largely empirical and not always satisfactory — as this review will demonstrate.

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Oesophageal problems

The classical symptoms of gastro-oesophageal reflux — heartburn and regurgitation — are more common in patients with diabetes than in the population at large. There is no difference in the prevalence of risk factors for reflux, such as hiatal hernia or reduced lower oesophageal sphincter function; the major defect in diabetes is that oesophageal peristalsis is impaired. At least in part, this is the result of neuropathy in the motor rather than the autonomic system, which leads to less effective clearance of refluxed acid from the oesophagus.[1,2] Fortunately, diabetic patients with gastro-oesophageal reflux respond well to proton pump inhibitors (and other conventional treatments).

Dysphagia due to impaired peristalsis is unusual but patients with diabetes, especially when glucose control is poor, are prone to odynophagia as a result of candida infection. Absence of oral thrush does not preclude fungal oesophagitis as only half of all patients with candida in the oesophagus have signs of infection in the mouth. The diagnosis is obvious at endoscopy, where creamy plaques on a reddish base are characteristic (Figure 2). Treatment with oral anti-fungal agents, such a fluconazole, is very effective and does not need to await mycological confirmation.

Diabetic gastroparesis

Acute hyperglycaemia itself can lead to short-term inhibition of gastric emptying in both diabetic and healthy subjects, but diabetic gastroparesis usually occurs in the setting of long-standing diabetes where there is evidence of end-organ damage, such as neuropathy, retinopathy and nephropathy.[3,4] The associated unreliability of gastric emptying may complicate the management of the blood glucose. In addition, the recurring symptoms can have a deleterious effect on fluid balance and nutrition, as well as on the bioavailability of oral hypoglycaemic agents, which can result in multiple hospital admissions.

The pathogenesis of diabetic gastroparesis is not well understood, but is related to abnormalities in both neuronal and humoral mechanisms. It is generally accepted that chronic hyperglycaemia contributes to neuropathic changes and dysfunctional innervation of the stomach. The resultant alterations in gastric myo-electrical function result in gastric dilatation, reduced peristalsis and delayed gastric emptying. Apart

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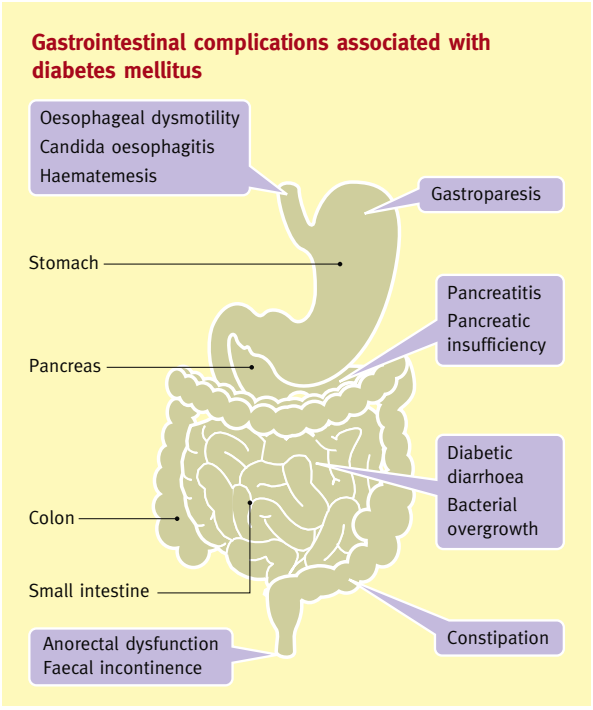


Figure 1



Figure 2 Candida oesophagitis seen at upper gastrointestinal endoscopy.

from disordered control of gastric motor function, it is clear that hyperglycaemia *per se* prolongs gastric emptying.

Symptoms of gastroparesis include post-prandial fullness, bloating and epigastric discomfort (though rarely pain). Early satiety, nausea and vomiting are frequent and the vomitus may contain food eaten many hours earlier. The severity of symptoms does not always correlate with the degree of gastroparesis.[5] Whereas a succussion splash can be demonstrated in severe disease, physical examination is often unhelpful. Although some patients are predisposed to the formation of gastric bezoars from indigestible food, many patients who have diabetes with measurable abnormalities of gastric emptying are asymptomatic.

The diagnosis of impaired gastric emptying is often apparent clinically but a dilated stomach may be seen on plain abdominal radiography. It is essential to consider other causes of delayed gastric emptying. A history of duodenal ulceration may suggest pyloric stenosis, whereas pain, anaemia and weight loss may indicate a distal gastric neoplasm. Upper gastrointestinal endoscopy is mandatory to exclude an anatomical cause for gastric outlet obstruction. A substantial gastric residue may be present despite prolonged fasting. There is an appreciable risk of aspiration during endoscopy, which is best performed after a prolonged (possibly 24-hour fast), so it may be safest to admit the patient to hospital for a day or so before endoscopy to allow IV fluids to be given. Other causes of gastroparesis (that may be more readily treatable) must be considered and excluded, and an accurate drug history is essential (Table 1).

Impaired gastric emptying may be seen with a barium meal examination but the value of this investigation in modern clinical practice is negligible. The most relevant investigation of gastric motor function that is widely available is radionuclide scintigraphy. Liquids and solids have differential rates of gastric emptying, and protocols for assessing emptying of the stomach vary between centres.[6] Data from radiolabelling of solid (as opposed to liquid) meals would seem likely to be helpful in clinical practice since, in diabetic gastroparesis, the impairment of emptying tends to be worse for solids. This technique might seem likely to offer valuable information but in practice its role is seriously limited by the lack of correlation between symptom severity and gastric emptying of the radiolabelled meal.

Treatment of diabetic gastroparesis is often a challenge. Selection of therapy is likely to depend on the frequency and severity of symptoms, the impact on diabetic control, the patient's state of nutrition, and the degree to which the condition interferes with their daily activities. Optimization of blood glucose with close control throughout the day and night is the cornerstone of treatment.[7] Even mild elevation of blood glucose is associated with altered antroduodenal motility and impaired gastric emptying. The range of subsequent treatment options includes dietary modification, pharmacotherapy and, ultimately, more invasive approaches where the condition proves refractory (Figure 3).

Foods high in lipids are known to reduce gastric emptying, so frequent small, low-fat meals are appropriate. Advising the patient to spread their daily food intake between four or five evenly spaced and evenly balanced meals is often helpful. Given that the rate of emptying of liquids in diabetic gastroparesis is usually less abnormal than that of solids, liquidized foods are worth a trial where solids are not tolerated. If neither solid nor liquid foods can be taken in sufficient quantity, enteral nutrients can be used to supplement standard meals.

While close attention to diabetic control and diet are essential, they are unlikely to be sufficient especially when symptoms are severe. Several drugs have prokinetic activity. The dopamine receptor antagonists, metoclopramide and domperidone, locally increase released acetylcholine at the myenteric plexus. Both drugs accelerate gastric emptying and improve symptoms of gastroparesis – at least in the short term. However, their efficacy over the longer term is less certain and there are issues of safety

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Causes of impaired gastric emptying

Central nervous system disorders	• Demyelinating diseases • Parkinsonism • Brainstem vascular disease or neoplasia • Acute physiological stress *e.g.* intensive care state • Spinal cord lesions including trauma, tumours & vascular disease
Autonomic neuropathies	• Diabetes mellitus • Amyloidosis • Paraneoplastic • Primary autonomic neuropathy
Metabolic disturbance	• Acute hyperglycaemia • Hypokalaemia • Hypothyroidism • Porphyria
Drugs	• Opioids • Anticholinergics • Nicotine • Levodopa • β-adrenoceptor agonists
Infiltrative conditions	• Systemic sclerosis • Amyloidosis
Others	• Post-vagotomy • Post-operative ileus • Radiation-induced • Idiopathic pseudo-obstruction • Myotonic dystrophy

Table 1

with their use (particularly the risks of dystonias with metoclopramide[8] and of cardiac arrhythmias with domperidone[9]). In addition, their efficacy over time may fall because of receptor down-regulation and consequent tachyphylaxis. The macrolide antibiotic, erythromycin, has agonist effects at motilin receptors by molecular mimicry, which explains the frequent gastrointestinal intolerance that occurs when it is used for treating infection. This unwanted effect has been turned to the advantage of patients with gastroparesis. Although erythromycin tablets are effective, there may be advantages to trying the suspension as it has greater bioavailability.[10] Intravenous administration seems even more effective although much less practical. Short-term benefits are established but sustained benefit is less certain. As with the dopamine antagonists, there are concerns about tachyphylaxis.

Several management options may be considered in those patients who fail adequately to respond to dietary and pharmacological therapy. Intra-pyloric injection of botulinum toxin at gastroscopy may decrease pylorospasm associated with gastroparesis, enabling some symptomatic improvement that may last for several months.[11] However, the evidence is based on uncontrolled studies; randomized trials have failed to confirm its effectiveness and current guidelines no longer recommend its use in the treatment of this condition.[4]

Sequential approach to management of diabetic gastroparesis

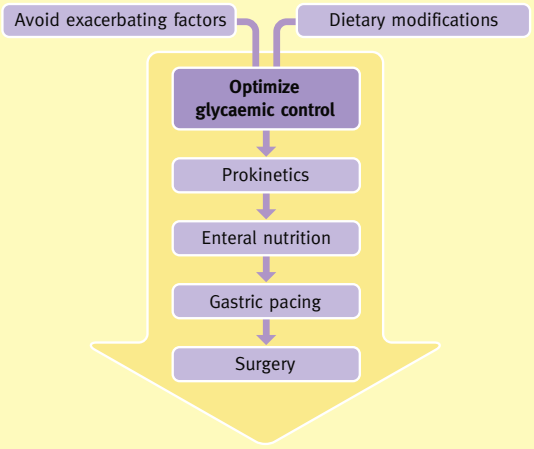


Figure 3

In diabetic gastroparesis where the neurohumoral control of gastric emptying is disordered, gastric electrical stimulation might seem to offer a real benefit.[8] These devices are inserted surgically to deliver high-frequency, low-energy electrical nerve stimulation to the stomach. Although the technique has become known as 'gastric pacing' and has proved successful in clinical practice, it does not lead to accelerated gastric emptying. The mechanism for its effectiveness remains uncertain but it probably enhances gastric accommodation and reduces sensitivity to gastric distension.[12] The impressive symptomatic response seen in a multi-centre trial is shown in Figure 4,[13] and its value has been confirmed through meta-analysis,[14] although careful case selection is important as the treatment is very expensive.

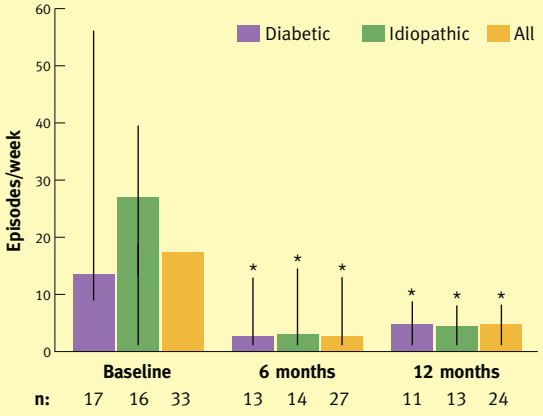
Attempts have been made to stabilize the situation where vomiting is seemingly intractable and delivery of adequate nutrition difficult. The use of a feeding jejunostomy — either via the naso-enteral route or sited percutaneously — is most helpful in re-establishing symptom control in the short term, especially where a period of in-hospital treatment has failed to control intractable vomiting.[15] However, it is unlikely to be acceptable to the patient as a long-term solution and, as with many of the treatments discussed, there is a paucity of comparative clinical trials to guide patient selection. Surgery is very definitely a last resort. Various gastric drainage procedures such as Polya gastrectomy and gastrojejunostomy have been tried — usually in desperation and with inconsistent results[16,17] — and such measures (if they are to be used at all) should be restricted to specialized centres.

Diabetic diarrhoea

Chronic diarrhoea is a complication most commonly associated with advanced insulin-dependent disease. It is characteristically intermittent, watery, tends to occur at night as well as during the day and may be associated with faecal incontinence in a third of patients. Significantly, the condition is painless; if abdominal pain is present, other diagnoses should be considered.

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Weekly vomiting frequency (median and interquartile range) at baseline, and changes at 6 and 12 months after the start of gastric electrical stimulation



*<0.05 vs baseline.

Adapted from Abell T, McCallum R, Hocking M, et al. Gastric electrical stimulation for medically refractory gastroparesis. *Gastroenterology* 2003; **125:** 421-8.

Figure 4

The clinical picture is often sufficiently typical for a confident clinical diagnosis to be made, and there are no diagnostic investigations. However, other causes of chronic diarrhoea, including bacterial overgrowth of the small bowel due to delayed transit, are seen more commonly in the diabetic population (Table 2), and the possibility that diarrhoea might be an adverse effect of medication should not be forgotten. Additional differential diagnoses range from such relatively common conditions as inflammatory bowel disease to more uncommon ones, such as carcinoid syndrome or VIPoma.

The cause of diabetic diarrhoea remains unclear. There is no consistent pattern of gut dysmotility: some patients seem to have prolonged gut transit with associated small bowel bacterial overgrowth while others have accelerated transit. The best that can be said is that the diarrhoea is multi-factorial, resulting from autonomic neuropathy, which affects gut transit, together with impaired net fluid absorption, possibly related to impaired adrenergic input. Since adrenergic nerves normally stimulate intestinal reabsorption of fluids and electrolytes, decreased intestinal reabsorption, rather than intestinal dysmotility *per se*, may be the dominant mechanism underlying diabetic diarrhoea.

Causes of persistent diarrhoea in patients with diabetes

- Medications, e.g. metformin, acarbose, miglitol
- Rapid intestinal transit
- Bacterial overgrowth
- Artificial sweeteners, e.g. sorbitol & mannitol
- Coeliac disease
- Pancreatic insufficiency
- Islet cell tumours
- Other causes of non-diabetic diarrhoea

Table 2

Having excluded other causes of diarrhoea (for which there is often a more satisfactory range of treatments), finding a successful therapy for the patient with diabetic diarrhoea can be a real challenge. Unlike gastroparesis, there is no compelling evidence that tightening control of the blood glucose has a specific benefit. Some authorities suggest that bulking agents are helpful but this is also not supported by evidence. Individual patients may note that specific foods seem to aggravate the diarrhoea, so trial exclusion diets, supervised if possible by dietitians, should be encouraged. There are no objective tests that will identify whether specific foods might aggravate symptoms.

It is appropriate to start with conventional anti-diarrhoeal drugs such as loperamide, diphenoxylate with atropine (Lomotil®) or codeine phosphate. Be prepared to increase the dosage of loperamide to the maximum recommended.

Establishing the diagnosis of small bowel bacterial overgrowth can be difficult. Hydrogen breath tests can be helpful but the diagnosis is best made by microbiological analysis of jejunal aspirates. As these tests are not widely available, it is entirely reasonable to suggest an empirical trial of broad-spectrum antibiotics such as co-amoxiclav.

In refractory cases, a trial of clonidine (the α-adrenoceptor agonist) has been recommended. The rationale is that enhanced α_2-mediated fluid and electrolyte uptake increases fluid reabsorption. Furthermore it increases colonic compliance and reduces rectal perception, which may diminish the sensation of urgency. Yet, as is seen so often in therapy of GI complications in diabetes, the early promise of benefit for clonidine in case studies[18] has not been confirmed in placebo-controlled trials.[19] In practice, the drug may induce orthostatic hypotension, particularly in those patients with impaired autonomic cardiovascular responses as a consequence of autonomic dysfunction. Other medications that have been tried include the somatostatin analogue, octreotide,[20] and the 5-HT_3 receptor antagonist, ramosetron, which has been shown to prolong colonic transit, inhibit small bowel secretion and decrease colonic compliance.[21]

Large bowel disorders

In diabetic clinics, constipation is seen more frequently than diarrhoea. As with constipation in the general population, there is a female preponderance but the condition is rarely severe. The aetiology is not well understood and is likely to be multi-factorial, but does appear to be associated with reduced function of the gastrointestinal pacemaker — the interstitial cells of Cajal.

As with diarrhoea, the evidence that tight glycaemic control improves symptoms is slight. Conventional treatments for constipation are usually effective. If response is poor, the possibility of underlying anorectal dysfunction should be considered, and patients with refractory constipation or faecal incontinence should be referred for anorectal physiological studies. Where drug therapy has failed, biofeedback is a viable option.

Looking forward

It is perhaps axiomatic to state that prevention of diabetic complications before they arise would be preferable to trying to find a

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successful treatment once they are fully developed. It also has to be said that the existing pharmacological options for diabetic gastroparesis and diabetic diarrhoea — particularly when symptoms are severe — are limited in both range and effectiveness. Some new drugs currently in development, such as those that influence 5-HT_4 receptors, neuronal nitric oxide synthase and, most recently, ghrelin receptor agonists, look promising but real progress in finding effective treatment is unlikely until we have a much better degree of understanding of gut pathophysiology in diabetes. ◆

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Gastroenterology in the elderly

Rajaratnam Mathialagan
Radhakrishnan Hariraj

Abstract
Gastrointestinal disorders represent the third most common cause of general practice consultations by patients older than 65 years in Western society. There are few changes within the gastrointestinal tract that occur inevitably as part of ageing. However, with increasing age, the incidence of both benign and malignant gastrointestinal disease rises. Although gastrointestinal disorders do not show particular characteristics in the elderly, when compared with younger adults, they may present with more severe symptoms due to co-morbidities and polypharmacy. Adverse reactions to non-steroidal anti-inflammatory drugs are more common in people aged over 65, and are a leading cause of hospitalization in this age group. Dysphagia and constipation are also more common, as is diverticular disease. Inflammatory bowel disease appears to show a second peak of onset between ages 60 and 80, and mesenteric intestinal ischaemia is largely confined to the elderly population. This article will review the reasons for these differences, where these are known, and consider aspects of diagnosis and management that are particularly relevant in elderly patients.

Keywords Chronic motility disorders; functional bowel disorders in the elderly; gastrointestinal disorders in the elderly; irritable bowel syndrome; mesenteric ischaemia; obscure GI bleeding; polypharmacy; upper GI bleeding

Upper gastrointestinal diseases

The prevalence of upper gastrointestinal (GI) disease increases in people aged 65 and over. Conditions such as gastro-oesophageal reflux disease, peptic ulcer and gastric cancer become more common with advancing age. Older individuals also tend to have a high burden of co-morbid factors, including *Helicobacter pylori* infection, and use of medication such as non-steroidal anti-inflammatory drugs (NSAIDs), bisphosphonates and corticosteroids.[1]

Unfortunately, in elderly patients with these disorders the symptoms may be mild or atypical, resulting in delayed diagnosis. The practitioner needs to maintain a high degree of clinical suspicion when presented with GI symptoms in this group of patients.

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Upper GI bleeding

Acute upper GI bleeding is a common and potentially life-threatening medical emergency. It is associated with higher rates of hospitalization, morbidity and mortality in the elderly, largely because of multiple co-morbidities. Age is also an independent risk factor for death from upper gastrointestinal bleeding, as are *H. pylori* infection, the use of NSAIDs and anticoagulation.

These patients require prompt risk assessment and resuscitation, followed by early endoscopy and endotherapy for haemostasis. Continued severe bleeding is an indication for radiological intervention or surgery in suitable patients.

Drug-induced GI disorders

Medical drug use increases with age and the elderly are at increased risk of adverse drug reactions. Multiple morbidities and polypharmacy are common in individuals during old age. Gastrointestinal symptoms resulting from either prescription medication or over-the-counter drugs are frequently encountered in geriatric practice, but often mistaken for a symptom of intrinsic organic disease, leading to over-investigation and over-treatment.[2]

NSAIDs (non-steroidal anti-inflammatory drugs)

Oral NSAIDs remain the most frequently prescribed medication in the UK for musculoskeletal disorders, such as osteoarthritis and chronic backache. Gastrointestinal manifestations, notably ulcers and bleeding, are the most common and life-threatening adverse effects associated with NSAIDs.

In the elderly NSAID-induced adverse effects have become a leading cause of hospitalization with increase in mortality from gastrointestinal ulceration more than fourfold. Up to half of NSAID induced gastroduodenal mucosal lesions may be asymptomatic.[3,4]

Proton pump inhibitors (PPI) and cyclo-oxygenase 2-selective NSAIDs may be used to mitigate against the adverse effects of conventional NSAIDs. Topical NSAIDs, with their reduced systemic absorption, may present a viable option for patients at increased risk of serious NSAID-related adverse events.[5]

Opioids

Pain is a common complaint in the elderly and opioids are useful agents for the management of both acute and chronic pain. Opioids are known to cause a variety of adverse GI effects, particularly constipation and these adverse effects can be particularly problematic for elderly patients.

Antibiotics

Physiological changes in the gut microflora of the elderly appear to manifest as proliferation of potentially pathogenic species at the expense of 'healthy' bacteria (lactobacilli and bifid bacterium). This altered balance has the potential to augment the risk of antibiotic-related adverse GI effects, including that of *Clostridium difficile* infection — although the latter can also appear as a sporadic illness with increased frequency in users of PPI therapy. *C difficile* infection can be severe in the elderly, and carries a high risk of recurrence and mortality.[6]

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Chronic GI motility disorder

Normal ageing is associated with various changes in GI motility but the clinical significance of such changes remains unclear. Large numbers of enteric neurones (the component of the autonomic nervous system that regulates GI motility) may be lost with age, but the GI tract remains surprisingly functional.

A major compounding factor in the interpretation of motor phenomena throughout the GI tract in this age group is the frequent co-existence of neurological, endocrinological and other diseases, which may be independently associated with defective motility. Furthermore, certain drugs commonly prescribed in the elderly can affect GI tract motility, including anticholinergics, antidepressants, opioid analgesics and calcium antagonists.

Dysphagia

Elderly individuals frequently suffer from oropharyngeal muscle dysmotility with dysphagia. Reduction in oesophageal peristalsis and low oesophageal sphincter pressure are also more common in the elderly, leading to dysphagia and gastro-oesophageal reflux disease. Although achalasia is generally an uncommon condition, it needs to be considered in the differential diagnosis. The combination of dysphagia and weight loss should prompt consideration not only of cancer but of an underlying neurological cause, such as motor neurone disease with bulbar involvement or Parkinson's disease.

Constipation

Constipation is one of the GI disorders most frequently encountered in clinical practice in Western society. It is more common in females and its prevalence increases with age. Abnormalities in innervation of the colon may play a significant role in changes in colonic motility, leading to delayed colonic transit in the elderly.

Evaluation of constipation begins with a detailed medical history and anorectal examination. Key self-management strategies include exercise, dietary modification and use of different laxatives to regularize the bowel habit, as appropriate. Simple bulking laxatives or stool softeners are usually effective and may need to be continued long-term.[7,8]

Iron deficiency anaemia

This topic will be discussed elsewhere in detail, so our comments are limited to some specific issues relevant to the older patient. Iron deficiency is the most common cause of anaemia worldwide and could be the first indicator of a more serious underlying condition.

Iron deficiency anaemia in the Western world, rather than being due to dietary factors, is more often a clue to occult upper and lower gastrointestinal lesions in the elderly.

Functional iron deficiency, which may occur in this age group secondary to acute or chronic inflammatory conditions, is diagnosed when the transferrin saturation is less than 20% in the presence of a normal or raised serum ferritin.

GI causes of iron deficiency, including atrophic gastritis, *H. pylori*-related gastritis and coeliac disease, should be considered in patients with otherwise unexplained iron deficiency. Several studies have shown that approximately 15–20% of patients with newly diagnosed coeliac disease are over the age of 65.[9]

The major cause of iron deficiency in elderly patients is blood loss, either overt or covert ('obscure'). Overt blood loss is by definition obvious manifesting as haematemesis, melaena, epistaxis or haematuria. It should prompt appropriate investigation, often with endoscopy or colonoscopy in the first instance.

Obscure GI bleeding

Obscure bleeding is defined as bleeding from the gastrointestinal tract that persists or recurs without an obvious cause after an upper GI endoscopy and colonoscopy (Table 1). This is notoriously difficult to diagnose. The evaluation of obscure GI bleeding includes a judicious search for the source of the bleed. This should be guided by the clinical history, and often the first-line investigation is a CT scan of the abdomen and pelvis. Capsule endoscopy should be reserved for patients where there is recurrent or transfusion-dependent anaemia. Additional investigations may, according to clinical indication, include push or balloon enteroscopy, angiography and intra-operative enteroscopy. In 15–20% of patients the underlying cause may remain undiagnosed but such patients can be reassured provided serious pathology has been excluded.[10]

Diverticular disease

Diverticular disease is very common in the elderly. It is present in 65% of 65 year-olds, and is asymptomatic in 80–85% of those affected. The remaining 15–20% may develop symptomatic diverticular disease, usually manifest as non-specific abdominal pain and intermittent rectal bleeding. A small minority, up to 5%, may develop complications that include diverticulitis, bleeding, obstruction, abscess formation and, rarely, fistulas. The sigmoid colon is involved in 90% of patients.[11]

Investigations – A plain radiograph is warranted in patients with suspected perforation. A CT scan is useful to evaluate diverticulitis with abscess or to exclude a collection. If indicated, a colonoscopy is perfectly safe in diverticular disease.

Treatment – In symptomatic uncomplicated diverticular disease the goal of treatment should be alleviation of symptoms and

Aetiology of obscure gastrointestinal bleeding[12]

Upper GI lesion	Lower GI lesion
Cameron's erosions	Angiodysplasia
Peptic ulcer	Neoplasm
Fundal varices	
Angiodysplasia	
Dieulafoy's lesion	
Gastric antral vascular ectasia	
Small intestinal bleeding	**Uncommon causes**
Tumours	Haemobilia
Angiodysplasia	Haemosuccus pancreaticus (Source of bleeding within pancreatic duct)
NSAID-induced enteropathy	
Coeliac disease	Aorto-enteric fistula
Dieulafoy's lesion	
Crohn's disease	
Meckel's diverticulum (consider in patients aged under 40)	

Table 1

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prevention of recurrent attacks. Several therapies have been proposed with variable success, including high fibre diet ± fibre supplementation, spasmolytics, probiotics, antibiotics and 5-ASA.

Inflammatory bowel disease (IBD)

Some studies suggest that IBD displays a bimodal age distribution at presentation with a possible second peak between 60 and 80 years. The symptoms in the elderly may not differ greatly from those in the younger adult age group, but are more likely to raise suspicion of diverticular disease, ischaemic colitis or bowel cancer.[13]

Patients with elderly onset IBD are more likely to present evidence of co-morbidities and polypharmacy than those diagnosed at a younger age, with likely implications for therapeutic decision making. The treatment of IBD in the elderly is generally similar to that in younger adults, but the therapeutic approach in the elderly should be 'start low, go slow'. Although, the indications for anti-tumour necrosis factor α (TNFα) agents in the elderly are generally similar to those for younger patients, lower response rates and a higher incidence of adverse events have been reported in the elderly. Adherence to the entire work-up before starting biologic treatment administration is very important. The safety profile of conventional immune modulators and biological therapy is acceptable for their routine use in suitable patients, but more data are required on the safe use of these drugs specifically in the elderly population. Failure of medical treatment for IBD is the most common indication for surgery in patients aged over 60 years, as for their younger counterparts.[14]

Mesenteric intestinal ischaemia

Acute mesenteric ischaemia refers to the sudden onset of small intestinal hypoperfusion. The pathogenesis is occlusive or non-occlusive obstruction of the arterial blood supply, or obstruction of venous outflow. Colonic ischaemia is more common but generally much less serious — usually resolving spontaneously within a few days.

Occlusive arterial obstruction may be due to acute embolism or thrombosis, and most commonly affects the superior mesenteric artery. Venous thrombosis results from obstruction of the intestinal venous outflow tract, including the superior and inferior mesenteric veins, splenic vein or portal vein. Non-occlusive mesenteric ischaemia is the result of a low-flow state and is most commonly seen with low cardiac output or the use of vasopressors.

Acute insufficiency of mesenteric arterial blood flow accounts for 60–70% of cases of mesenteric ischaemia; where it causes small bowel ischaemia, the mortality rate exceeds 60%. For patients with acute symptoms rapid diagnosis is imperative since the clinical consequences can be catastrophic, including sepsis, intestinal infarction and death. The diagnosis depends upon a high degree of clinical suspicion, especially in patients with risk factors, such as atrial fibrillation, heart failure, peripheral vascular disease or a history of hypercoagulability. Most patients show signs of peritonism with a raised plasma lactate. Multi-detector CT angiography without oral contrast is the initial imaging modality of choice for evaluating haemodynamically stable patients with acute abdominal pain and clinical features suggestive of acute mesenteric ischaemia. However, mesenteric arteriography remains the gold standard diagnostic study for acute arterial ischaemia, and should be performed in patients in whom a high degree of clinical suspicion remains after a negative CT angiogram. Urgent surgical review should also be sought.

The initial management of patients with acute intestinal ischaemia includes aggressive haemodynamic monitoring and support, correction of metabolic acidosis, initiation of broad-spectrum antibiotics and placement of a nasogastric tube for gastric decompression. Once these steps have been taken, the goal is to restore intestinal blood flow as rapidly as possible.[15]

Chronic mesenteric ischaemia usually develops in patients with mesenteric atherosclerosis. These patients complain of recurrent post-prandial abdominal pain, which is due to their inability to augment intestinal blood flow to meet the demand of digestion. These patients may develop 'food fear' and lose a considerable amount of weight. A high index of clinical suspicion is crucial to making this diagnosis.

The 'watershed areas' at the junctions of the supply territories of the major intestinal arteries — the splenic flexure (superior mesenteric artery) and rectosigmoid junction (inferior mesenteric artery) — are most susceptible to ischaemia.

The diagnosis of chronic mesenteric ischaemia is supported by the imaging demonstration of high-grade stenosis in mesenteric arteries. Physical findings, apart from weight loss, are usually minimal. Abdominal examination may reveal an aortic bruit in approximately 50% of patients. Therapeutic options for patients with symptoms thought to be attributable to chronic mesenteric ischaemia include surgical reconstruction and percutaneous transluminal angioplasty, with or without placement of a stent.[16] ◆

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Clinical Review

Clinical Review identifies issues in the medical literature of interest to clinicians in Africa. Essential references are given at the end of each section

Family Medicine Review

Responding to health risks

Prevention of diseases through modifying risk is a worthy aim that should hold a major place in the focus of most healthcare professionals, but particularly those who work in primary care. It may be that I have been noticing an increasing emphasis on risk factors, in relation to a range of problems and conditions, in the literature that I scan, simply because I have been giving more attention to it myself, or because I have a Masters' student embarking on a study looking at the risks associated with mothers giving birth prior to arrival at a healthcare facility. Whatever the reason, there have been a number of interesting articles published recently on the issue of health risks that I want to highlight.

Walker et al recently published a systematic review to identify randomised controlled trials of cancer risk assessment tools used in primary care.[1] The rationale behind such tools is that risk-stratified screening for cancer as opposed to population-based cancer screening programmes (e.g. for breast, colorectal and cervical cancer) is being proposed as a way of reducing both harm and costs by focusing on populations at higher risk of cancer. Risk-stratified cancer prevention requires risk assessment tools that can be used in primary care to identify those most likely to benefit from such a programme by estimating a person's likelihood of developing different cancers by assessing a combination of genetic, environmental and behavioural risk factors, including risk factors. The review included 11 trials of 7 risk tools. The findings of the review suggest that cancer risk assessment tools improve the accuracy of patients' risk perception and knowledge without causing an increase in cancer-specific anxiety. Health promotion messages within the tools positively influenced behaviour change, especially in terms of changes in diet and physical activity. They also increase intentions to have cancer screening, but it was not clear if they lead to actual increased screening activity.

I want to digress slightly from risk factors to share an important article on screening for cervical cancer, the commonest cancer amongst African women. Fallala and Mash report on the safety, acceptability and feasibility of visual inspection with acetic acid and cervicography (VIAC) followed by definitive management (using cryotherapy or a loop electrical excision procedure) at a single visit for the prevention of cancer of the cervix in Zimbabwe.[2] Visual inspection with acetic acid (VIA) has been suggested as an alternative method of screening for cervical disease, with a similar sensitivity to Pap smears for the detection of high grade cervical lesions in HIV-infected women, and a number of resource-limited countries are expanding cervical cancer screening using the VIA screening method.[3] The important conclusion of the Zimbabwe study was that the service was feasible to sustain over time despite the constraints of the context; there were no service-related treatment postponements and the clinic staff and facility were able to meet the demand for the service. They followed up after one year and outcomes suggested that treatment had been effective. This is in keeping with another recent study describing the VIAC programme of the Cervical Cancer Prevention Programme in Zambia.[4] Primary care clinicians in Africa would be well-advised to become familiar with and support such screening programmes.

Returning to risk factors, there have been articles published on a wide range of different problems. I will highlight but a few. Rodriguez and Agbo looked at risk factors for pulmonary tuberculosis (PTB) amongst HIV-positive patients in Mpumalanga, South Africa.[5] Single marital status, living in dusty outdoor environment, and moderate to heavy alcohol consumption were strongly associated with an increased risk of PTB among HIV-positive patients. On the other hand, age, gender, educational and employment status, overcrowding, previous medical history of PTB or treatment, and a family history of PTB were shown not to be associated with PTB. These findings may not be generalisable, but make the point that it is wise to understand the specific risk factors in a particular context so that targeted interventions can be developed.

The issue of hypertension in relation to HIV is important. In rural South Africa, where there is a high prevalence of both HIV and hypertension, it is inevitable that some people will be affected by both conditions, but no interaction was found between these in a recent cross-sectional study.[6] However, the presence of HIV has an adverse effect on high-density lipoprotein cholesterol and triglycerides, suggesting that people living with HIV may be at increased risk of cardiovascular disease, so that screening for such is essential in these patients. However, a Ugandan study amongst young adults found that hypertension was significantly associated with the older age-group, male sex and obesity, but there was a significantly lower prevalence of hypertension among participants with HIV,[7] suggesting that blood pressure measurement is not an effective way to identify cardiovascular risk in HIV positive patients.

On a different note, a study looking at unintended births among unmarried adolescent girls in Nigeria found that adolescent girls from households headed by young adults were more likely to experience adolescent pregnancy than those from households headed by older adults. Older adults were more likely to be wealthier and have higher educational status, which decreased unintended births. Interestingly, adolescent girls from female-headed households were also less likely to experience unwanted pregnancy.[8]

What about risks in children? Van der Linde et al looked at risks for communication delays in infants from underserved communities attending primary healthcare

facilities in Tshwane district, South Africa.[9] Communication delays were present in 13% of infants, and more than one-third were at risk of developing communication delays in future. Infants with two or more siblings, born from mothers aged 18–29 years who own their house, had a 39% chance of presenting with communication delays. The authors argue that preventative strategies such as the implementation of a risk profile and a communication development screen should be implemented. This study highlights the importance of developmental screening in primary care, which is not given sufficient attention by clinicians. In South Africa the only nationally implemented developmental screening tool is integrated as part of the Road to Health Booklet, but a recent study indicated it failed to identify more than half the infants at risk of delays or disorders, thus making it ineffective.[10] The authors of the latter study suggest that the Parents' Evaluation of Developmental Status tool provides an alternative, validated screening tool that is cost-effective in resource constrained environments because it is parent administered. Clinicians working in primary care, obstetrics and paediatrics should take a lead in ensuring that effective screening programmes are introduced into African communities in order to prevent the substantial burden of developmental disability.

The earlier cited study on hypertension in young patients in Uganda referred to a low level of awareness of the condition amongst people identified with hypertension. A study in the Western Cape, South Africa, investigated the knowledge and perceptions about risk for cardiovascular disease (CVD) in a low-income peri-urban community, using focus group discussions.[11] Participants' knowledge of CVD and its risk factors varied, but most were familiar with cardiovascular conditions such as hypertension and stroke, and with some lifestyle factors that cause CVD such as high-fat diets and excessive alcohol consumption. However, understanding of the concept of risk was poor. The authors describe their perception of risk as a binary concept: a cardiovascular event was either going to happen or not, depending on high- or low-risk; the lack of primary understanding of risk prevented an evaluation of different narrative and visual methods of presenting risk as originally intended in the study.

It is thus crucial that primary care clinicians address issues of risk in a way that patients understand and that leads to impacts on their behaviour. But how do we do this? Malan et al published an exploratory study that describes a model for training primary care providers provide individual brief behaviour change counselling using a standardised approach as part of everyday primary care.[12] They designed a new training programme based on a conceptual model that combined the commonly used 5As (ask, alert, assess, assist and arrange) with a guiding style derived from motivational interviewing. This eight-hour training programme for either clinical nurse practitioners or primary care doctors combined theory, modelling and simulated practice with feedback. The outcomes have yet to be evaluated, but the paper highlights the importance of giving attention to equipping clinicians to be effective in addressing the issues of risk with patients.

Responding to disability

I want to return to some of the issues highlighted when discussing communication difficulties by touching on three articles that have recently brought the issue of disability into focus; the first of these specifically related to communication disability. A commentary from Fiji noted that people with communication disability (PWCD) are more likely to be excluded from society, and denied their basic human rights, than other people, even those with another disability.[13] In describing the drivers for change at three levels, the authors point out that at the micro level it is service providers in the education and health sectors, working together with consumer representatives and the general community, that need to drive the change. They note that prior to school entry, services for children with speech, language and literacy difficulties are the responsibility of the Fijian Ministry of Health, but the provision of specialist rehabilitation services for PWCD is not presently a primary goal of the ministry, whose focus is on reducing child mortality rates. Thus speech-language pathology services are not currently available to support children prior to school entry, nor at any time for adults who have acquired communication and/or swallowing difficulties. It is likely that this is common in Africa. Once again, linking to what was said about developmental screening, we as clinicians need to become advocates for our patients and communities, and thus should support the development of such services.

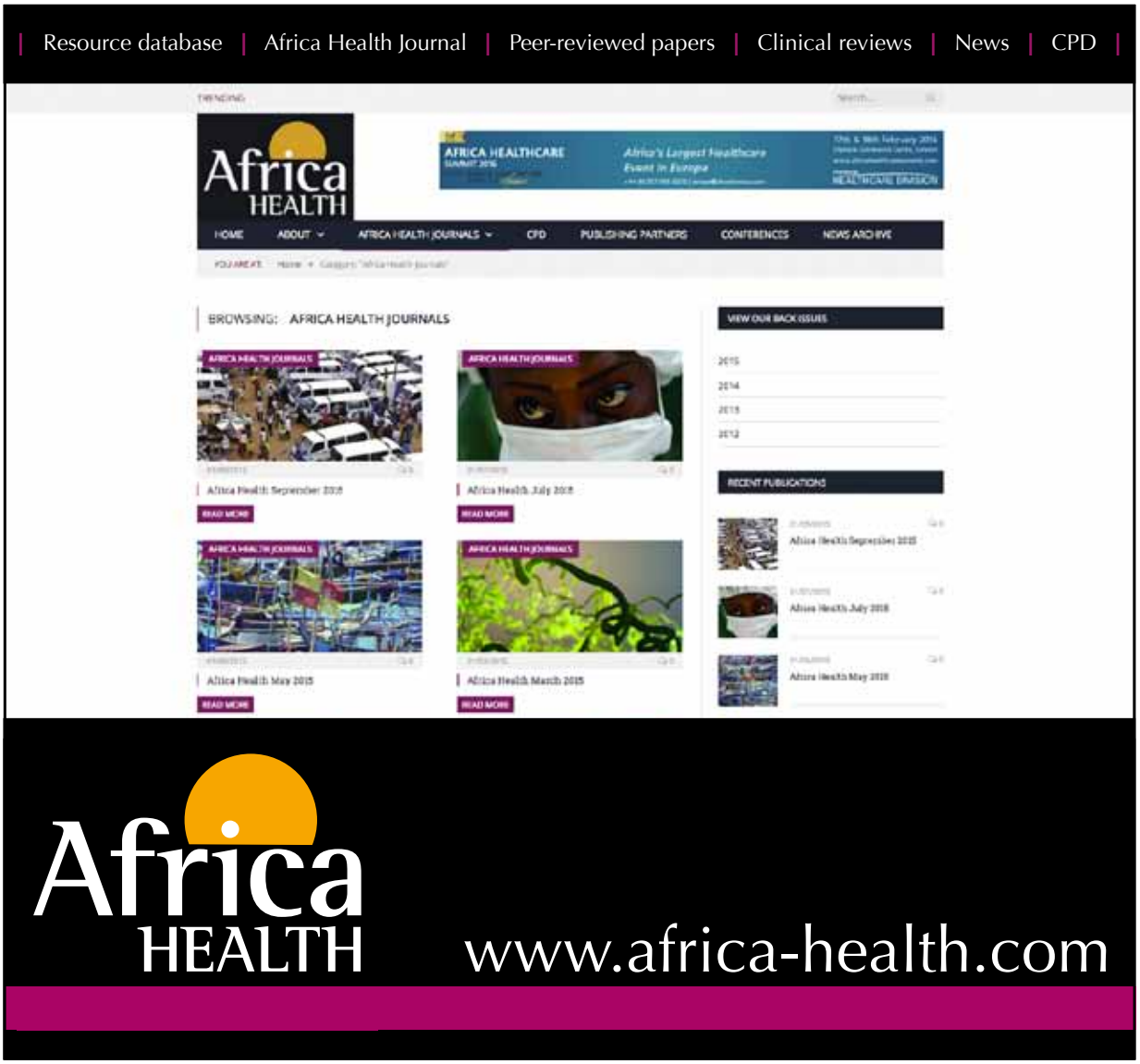
It is not only children who are affected. A study in Mpumalanga, South Africa, found that the experience of living with a disability in a rural area is associated with discrimination, social exclusion, isolation and barriers to accessing services.[14] Barriers to service provision extend beyond physical obstacles, and include a variety of sociocultural and sociopolitical barriers. Unless these are considered, policies and service models are only able to provide limited support to people with disabilities living in rural areas.

One strategy for addressing disability care and support that has been used in many developing countries is through community-based rehabilitation, with training and development of community disability workers (CDWs). Lorenzo et al analysed the work of CDWs in three southern African countries to demonstrate the competencies that these workers acquired to make a contribution to social justice for persons with disabilities and their families.[15] They found that the CDWs demonstrated competencies in three main areas: integrated management of health conditions and impairments within a family focus; negotiating for disability-inclusive community development; and coordinated and efficient intersectoral management. (These should be familiar to family physicians, though the context is slightly different.) The CDWs were committed to fighting the inequities and social injustices that persons with disabilities experienced, and they facilitate the multiple transitions experienced by the families at different stages of the disabled person's development. It is critical that clinicians interact with and support CDWs in such efforts.

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(See page 40)

Part one

Part two

Part three/ four

Q1 (c) The sudden onset of respiratory distress in a child of this age must raise the question of an inhaled foreign object. Daniel is becoming a little old for bronchiolitis: asthma may present in this way but is much less likely than an inhaled foreign object. This is not likely to be a bacterial infection, which would make him much more ill and would not resolve so quickly.

Q2 (a), (b), and (c) are serious mistakes which might lead to a fatal outcome for the child (see answers to Q4!) In a large study of children with foreign body inhalation around 20 per cent had normal chest X-rays. Remember that Daniel's mum is on her own and can't be expected to supervise him all the time. He plays often with his big sister, so that accidental inhalation of a foreign object is perfectly possible – and would be unreported.

Q3 (c), (d). These examinations should be done only by an experienced paediatric ENT surgeon well versed in dealing with inhaled objects. Epiglottitis and laryngitis are a possible complication of an inhaled object, and using a tongue depressor and trying to view the epiglottis with a standard laryngoscope may provoke acute spasm that can be fatal. (a), (b) and (e) are disastrous answers.

Q4 (b), (c), (d), (e), and (f) are all complications of undetected foreign body inhalation. Daniel was fortunate: he had a piece of a small plastic toy lodged at the division of his trachea. It was removed through an endoscope, and he recovered completely. He is back to his normal active and very friendly self.

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Cardiovascular

Safety and efficacy of digoxin

In the past, digoxin has been routinely used to treat heart failure and atrial fibrillation. However, since a study reported an increase in mortality rates associated with digoxin use, the prescribing of it has declined.

A recent systematic review of over 70 observational studies and randomised trials aimed to clarify this finding. Researchers assessed whether digoxin increased all-cause mortality or adverse clinical outcomes compared with placebo.

The meta-analysis had a combined total of over 4 million patient-years of follow up. Although the results from pooled observational studies showed an increased risk of death with digoxin (risk ratio, 1.6), the more robust data from randomised trials showed there was no difference in all-cause mortality between digoxin and placebo. Further analysis showed digoxin led to a small but significant reduction in hospital admission (risk ratio, 0.92).

Digoxin is associated with a neutral effect on mortality and a lower rate of admissions to hospital.

Ziff J, Lane A, Samra M, et al. Safety and efficacy of digoxin: systematic review and meta-analysis of observational and controlled trial data. *BMJ* 2015, 351, h4451.

Cancer screening following venous thromboembolism

Unprovoked venous thromboembolism (VTE) may be the earliest sign of cancer in around 10% of affected patients. Clinicians will often investigate these cases to detect an occult cancer, but the variation in practice is great. A recent randomised trial assessed the efficacy of two screening strategies at detecting occult cancers.

The trial randomised 850 patients to receive either limited occult cancer screening (blood testing, chest radiography, and breast, cervical, or prostate cancer screening) or limited screening plus computed tomography (CT) scanning. Researches aimed to quantify the number of cancers that screening did not detect and were subsequently diagnosed within 12 months.

Following screening, 14 of the 431 (3.2%) patients in the limited-screening group and 19 of the 423 (4.5%) patients in the CT group had an occult cancer diagnosed. Four occult cancers (29%) were missed by the limited screening, whereas five (26%) were missed by the CT screening – a non-significant difference.

For patients with unprovoked VTE, routine screening plus CT scans did not increase the detection of occult cancers.

Carrier M, Lazo-Langner A, Shivakumar, et al. Screening for occult cancer in unprovoked venous thromboembolism. *NEJM* 2015; 373: 697–704.

Antidote for dabigatran reversal

Dabigatran is an effective alternative to warfarin, but in the case of acute haemorrhage no antidote exists to reverse its anticoagulation action. Now a monoclonal antibody, idarucizumab, has been developed and may be able to reverse dabigatran's action. A phase one trial to test idarucizumab's safety and efficacy has been reported.

In total, 47 healthy adult volunteers were assigned in a 3:1 ratio to receive idarucizumab or placebo. All participants were prescribed seven doses of dabigatran (220 mg) over 4 days. To reverse the dabigatran-induced anticoagulation, intravenous idarucizumab (1–4 g, or 5 g plus 2.5 g after 5 min) was infused. Researchers monitored adverse reactions, and they also measured the reversal of thrombin time, clotting time, activated partial thromboplastin time, and thrombin time.

Drug-related adverse events occurred in seven participants and were all mild (infusion site erythema, epistaxis, haematuria, and haematoma). Idarucizumab immediately and completely reversed dabigatran-induced anticoagulation in a dose-dependent manner.

Idarucizumab caused an immediate, complete, and sustained reversal of dabigatran-induced anticoagulation without significant safety concerns.

Glund S, Stangier J, Schmohl M, et al. Safety, tolerability, and efficacy of idarucizumab for the reversal of the anticoagulant effect of dabigatran in healthy male volunteers: a randomised, placebo-controlled, double-blind phase 1 trial. *Lancet* 2015; 386: 680–690.

Infectious Disease

New cholera vaccine

Cholera is a major public health problem across many low-income countries, including much of Africa. A cholera vaccine has been available for purchase by UN organisations for 15 years, but its use in low-income countries has been limited, in part due to high costs. Now a newer and cheaper two-dose, oral cholera vaccine has been produced. To test its efficacy a study has been conducted in Bangladesh where cholera is endemic.

Researchers randomised over 250 000 people in poor urban population clusters to receive either no intervention, vaccination only, or vaccination plus behavioural change (education on safe drinking water and hand-washing). The primary outcome measured protected effectiveness against severe cholera 2 years after vaccination.

The coverage of the interventions among the groups ranged from 65–66%. The overall protectiveness was 37% in the vaccination group and 45% in the vaccination plus education group. Although the protection between the two groups was non-significant, both offered significantly more protection than the non-intervention group.

This new cholera vaccine reduced the burden of severe cholera.

Qadri F, Ali M, Chowdhury F, et al. Feasibility and effectiveness of oral cholera vaccine in an urban endemic setting in Bangladesh: a cluster randomised open-label trial. *Lancet* 2015; 386: 1362–1371.

Ebola post-exposure prophylaxis

Accidental exposure to the Ebola virus for healthcare workers is a real and serious problem. There is an urgent need for a consensus regarding the risk assessment of Ebola virus transmission after exposure and to investigate the use and efficacy of post-exposure prophylaxis (PEP).

A hospital in London has devised a risk assessment and management algorithm for healthcare workers potentially exposed to the Ebola virus in west Africa. It also developed PEP using antiviral agents including favipiravir, tenofovir disoproxil fumarate, emtricitabine, raltegravir, and monoclonal antibodies. Participants were followed for 42 days after potential exposure.

Of the eight healthcare workers exposed to the Ebola virus, four were classified as having had low-risk exposures and were managed by watchful waiting. The remaining four individuals had intermediate (n=2), or maximum (n=2) risk exposures and were given PEP. None of the eight healthcare workers developed Ebola virus disease.

A standardised risk assessment algorithm should be adopted and guidelines developed to study the safety and efficacy of PEP.

Jacobs M, Aarons E, Bhagani S, et al. Post-exposure prophylaxis against Ebola virus disease with experimental antiviral agents: a case-series of healthcare workers. *Lancet Infectious Diseases* 2015; 15: 1300-1304.

Rapid, point-of-care testing for Ebola

Currently, a diagnosis of Ebola virus disease must be made in the laboratory using real-time RT-PCR which is time

consuming and complex. A point-of-care rapid diagnostic test kit, Corgenix ReEBOV Antigen Rapid, has now been developed. It requires little training and can use blood from fingerstick or venepuncture.

To test the accuracy of ReEBOV, a study has compared the diagnostic results from the gold-standard laboratory RT-PCR testing with ReEBOV among 28 patients with suspected Ebola and tested at point-of-care. For further comparison, 284 samples held in a reference laboratory were also tested.

In point-of-care testing, all 28 patients who tested positive for Ebola using RT-PCR were also positive using ReEBOV (sensitivity 100%). Further, 71 of 77 patients with negative RT-PCR tests were also negative by the ReEBOV (specificity 92%). The laboratory tests reproduced the same sensitivity and specificity as obtained with the point-of-care testing.

The ReEBOV rapid diagnostic test had 100% sensitivity and 92% specificity.

Broadhurst J, Kelly D, Miller A, et al. ReEBOV Antigen Rapid Test kit for point-of-care and laboratory-based testing for Ebola virus disease: a field validation study. *Lancet* 2015; 386: 867–874.

Neurology

Efficacy of antidepressants in adolescents

An influential trial published in 2001 investigating the efficacy and harms of antidepressants in adolescents provided evidence for their positive efficacy. However, some of the conclusions drawn from the study are feared to be 'at odds with the data'. Therefore, the primary data for this trial have now been re-analysed.

The initial study's objective was to compare the safety and efficacy of paroxetine and imipramine with placebo in the treatment of unipolar depression among 275 adolescents. The endpoint measured the proportion of responders with a 50% reduction in the Hamilton depression scale questionnaire score.

Re-analysis revealed that the efficacy of paroxetine and imipramine was not statistically or clinically significantly different from a placebo. Further, there were significantly increased risks of suicidal ideation and suicidal behaviour.

Contrary to the initial trial's findings, re-examination of the data showed neither paroxetine nor high-dose imipramine was efficacious for major depression in adolescents.

Noury L, Nardo M, Healy D, et al. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. *BMJ* 2015; 351: h4320.

Intravenous versus oral steroids for multiple sclerosis relapses

Multiple sclerosis (MS) is characterised by an inflammatory process in the central nervous system and is associated with relapses. When relapses occur, treatment with high-dose intravenous corticosteroids has proven effective. However, it remains unknown whether oral corticosteroids which are cheaper, simpler and less invasive have equal efficacy.

To assess this, a non-inferiority, randomised trial recruited adults with relapsing-remitting MS who had suffered a recent relapse. Each patient was then randomised to receive either oral or intravenous methylprednisolone, 1000 mg, once daily for 3 days. The primary endpoint measured the proportion of patients who reported improved function by day 28.

Of the 82 patients assigned to the oral group, 66 (81%) achieved the primary outcome, compared with 72 of 90 patients (80%) in the intravenous group, yielding a non-significant treatment difference. Rates of adverse events were similar between the groups.

Oral administration of methylprednisolone was not inferior to intravenous administration for relapses of MS.

Le Page E, Veillard D, Laplaud D, et al. Oral versus intravenous high-dose methylprednisolone for treatment of relapses in patients with multiple sclerosis (COPOUSEP): a randomised, controlled, double-blind, non-inferiority trial. *Lancet* 2015; 386: 974–981.

Recurrent intracranial haemorrhage and blood pressure

Intracerebral haemorrhage (ICH) is the most severe form of stroke and survivors are at high risk of recurrent ICH. The control of elevated blood pressure (BP) is the cornerstone of secondary prevention. However, there is limited evidence to show a reduction in BP reduces the incidence of recurrence.

A longitudinal study investigated this further by following over 1100 ICH survivors to monitor their BP and record recurrent ICHs. The authors classified recurrent ICH as either lobar (cortex and white matter) or nonlobar (thalami, basal ganglia, or brainstem).

Results revealed the event rate for lobar ICH was 84 per 1000 person-years among patients with inadequate BP control compared with 49 per 1000 person-years among patients with adequate BP control. The nonlobar ICH event rate was 52 per 1000 person-years with inadequate BP control and this was almost halved in patients with adequate BP control.

Inadequate BP control after an ICH was associated with a higher risk of recurrence.

Biffi A, Anderson D, Battey K, et al. Association between blood pressure control and risk of recurrent intracerebral haemorrhage. *JAMA* 2015; 314: 904–912.

Obstetrics

Antidepressants and persistent pulmonary hypertension of the newborn

Persistent pulmonary hypertension of the newborn (PPHN) is a serious condition resulting in high morbidity and mortality. In 2006 a public health notice warned of an increased risk of PPHN associated with late pregnancy exposure to selective serotonin reuptake inhibitors (SSRIs).

A new study has investigated the risk of PPHN associated with exposure to different antidepressant medications in late pregnancy (90 days before delivery). The researchers conducted a cohort study using data from over 3 million pregnant women across the USA.

A total of 130 000 (3.4%) of the cohort were taking antidepressants in late pregnancy, the majority of whom were prescribed SSRIs. Overall, the rate of infants diagnosed with PPHN and not exposed to antidepressants was 21 per 10 000 births, compared with 32 per 10 000 infants exposed to SSRIs and 29 per 10 000 for non-SSRIs.

There is an increased risk of PPHN associated with maternal use of SSRIs in late pregnancy, however the absolute risk remains small.

Huybrechts F, Bateman T, Palmsten K, et al. Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn. *JAMA* 2015; 313: 2142–2151.

Iron supplementation in pregnancy

Anaemia affects most African women during pregnancy and is most commonly due to iron deficiency. By taking iron supplements the risk of anaemia is reduced and is therefore recommended for all women in pregnancy. However, some studies have also suggested that iron supplementation in children can increase the rates of infectious diseases including malaria.

Therefore, a Kenyan trial has assessed the effect of antenatal iron supplementation on both maternal Plasmodium

infection risk and neonatal outcomes. It randomly assigned pregnant women to receive either 60 mg of ferrous fumerate daily (n=237) or placebo (n=233) until 1 month postpartum.

Results showed there was no significant difference in maternal Plasmodium infection risk between the two groups (52% in iron group, 52% in placebo group). However, average birthweight was significantly higher in the iron group (3202 g) compared with the placebo group (3053 g). Iron supplementation also significantly increased maternal mean haemoglobin.

Administration of daily iron supplementation during pregnancy did not alter maternal Plasmodium infection risk.

Mwangi M, Roth J, Smit M, et al. Effect of daily antenatal iron supplementation on Plasmodium infection in Kenyan women: a randomized clinical trial. *JAMA* 2015; 314: 1009–1020.

Predicting postnatal depression

Perinatal depression is a neglected global health priority. It affects 10–15% of women in high-income countries and has a greater burden on low-income countries. However, it is unclear to what extent women diagnosed with perinatal depression have a history of mental health problems prior to conception.

An Australian cohort study has now published research investigating this question. Authors analysed data from biannual mental health status questionnaires from almost 400 pregnant women that spanned from late childhood to after the delivery.

A total of 253 (66%) participants in the cohort had a previous history of a mental health problems. Of these, 117 had pregnancies, and perinatal depressive symptoms were reported in 57 (34%) of these pregnancies. In contrast, 8% of the 201 pregnancies with no preconception history of mental health problems reported perinatal depressive symptoms (odds ratio, 8.36).

Perinatal depressive symptoms are mostly preceded by mental health problems that begin before pregnancy.

Patton C, Romaniuk H, Spry E, et al. Prediction of perinatal depression from adolescence and before conception (VIHCS): 20-year prospective cohort study. *Lancet* 2015; 386: 875–883.

Paediatrics

Time to adrenaline injection in cardiac arrest

Cardiac arrest causing a non-shockable rhythm among children results in a mortality of 25–40%. Adrenaline (epinephrine) is recommended for the management of this paediatric emergency. Although evidence shows that a delay to the first adrenaline dose in an adult cardiac arrest is associated with decreased survival, it is unknown whether this remains true for children.

Therefore, paediatric cardiac arrest data were reviewed from across the USA. All children (<18 years) with a non-shockable rhythm and treated with adrenaline were included. The time to adrenaline administration and the survival to hospital discharge were analysed.

Of the 1558 children suffering cardiac arrest, 487 (31%) survived. The median time to adrenaline administration was 1 minute. A longer time to adrenaline administration was associated with a lower risk of survival to discharge, and decreased chance of a favourable neurological outcome.

A delay in administration of adrenaline to children in cardiac arrest was associated with a decreased survival.

Andersen W, Berg M, Saindon Z, et al. American Heart Association get with the guidelines–resuscitation investigators. Time to epinephrine and survival after paediatric in-hospital cardiac arrest. *JAMA* 2015; 314: 802–810.

Oxygen therapy for severe pneumonia

Developed countries widely use continuous positive airway pressure (CPAP) for children with severe pneumonia which yields favourable outcomes. However, CPAP requires expensive equipment that is often not available in many developing countries. Bubble CPAP (using tubing submerged in water to deliver oxygen) may be a viable and low-cost alternative for low-resource setting.

A recent trial in Bangladesh assessed whether oxygen therapy could be successfully delivered through bubble CPAP for children with severe pneumonia and hypoxaemia. The outcome measured treatment failure (death, mechanical ventilation, intubation, or clinical failure in the CPAP group) compared with oxygen therapy delivered through high- or low-flow nasal cannulas.

Of the 79 children assigned to the bubble CPAP group, only 5 (6%) had treatment failure. A total of 16 (24%) out of 67 who received low-flow oxygen and 10 (13%) of the 79 children who received high-flow oxygen had treatment failure. Significantly fewer children died in the bubble CPAP group than in the high- and low-flow groups.

Bubble CPAP improved the outcomes in children with very severe pneumonia and hypoxaemia.

Chisti J, Salam A, Smith H, et al. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. *Lancet* 2015; 386: 1057–1065.

Oxygen saturation targets for bronchiolitis

The most common lower respiratory tract infection of early life is viral bronchiolitis. Part of the management includes giving supplementary oxygen. However, the optimal oxygen saturation target to provide the best outcome is disputed.

Therefore, a recent trial assessed whether a target saturation of 90% or higher for oxygen supplementation resulted in equivalent outcomes to a normotoxic (94% or higher) target among infants with bronchiolitis. A total of 615 infants (aged 6 to 52 weeks) diagnosed with viral bronchiolitis were randomised to have either 90% (standard group) or 94% (modified group) target saturations. The primary outcome measured time to resolution of cough.

The median time to cough resolution was 15 days for each group. There were 35 serious adverse events recorded in the standard group compared with 25 in the modified group.

Management of infants with bronchiolitis to an oxygen saturation target of 90% or higher is as safe and effective as one of 94% or higher.

Cunningham S, Rodriguez A, Adams T, et al. Oxygen saturation targets in infants with bronchiolitis (BIDS): a double-blind, randomised, equivalence trial. *Lancet* 2015; 386: 1041–1048.

Intermittent hypoxaemia and bradycardia in preterm infants

Extremely preterm infants (<28 weeks gestation) experience intermittent hypoxaemia and bradycardia for many weeks after birth. The consequences of these episodes remain undetermined but there may be a link between hypoxaemia or bradycardia and late death or disability. A recent study investigated this hypothesis.

Researchers monitored each of the 1019 infants (gestational age 23–27 weeks) for episodes of hypoxaemia (oxygen saturations <80%) or bradycardia (pulse <80/min) for 10 seconds or longer. The primary outcome was a composite of death, motor impairment, cognitive or language delay, hearing loss, or blindness at 18 months of age.

The primary outcome was present in 414 infants (42.6%). Hypoxaemic episodes were associated with an increased risk of late death or disability

in 56.5% of those infants in the highest decile of hypoxaemic exposure and 37% of those in the lowest decile. Intermittent bradycardia did not add to the risk of an adverse outcome.

Prolonged hypoxaemic episodes in preterm infants were related to adverse 18-month outcomes.

Poets F, Roberts S, Schmidt B, et al. Canadian Oxygen Trial Investigators, 2015. Association between intermittent hypoxemia or bradycardia and late death or disability in extremely preterm infants. *JAMA* 2015; 314: 595–603.

Public Health

Sweet drinks and type 2 diabetes

It is now thought that the consumption of sugary and artificially sweetened drinks is likely to increase the likelihood of developing type 2 diabetes and obesity. However, few prospective studies have been conducted on this subject.

Therefore, a systematic review and meta-analysis was performed. The objective was to examine the relationship between consumption of sugar-sweetened drinks, artificially sweetened drinks, and fruit juice with the development of type 2 diabetes. The researchers also adjusted for adiposity.

A total of over 10 million person-years of data analysed from 17 cohort studies. Results demonstrated a higher consumption of sugar-sweetened drinks was associated with 13% greater incidence of type 2 diabetes per one serving/day, even after adjustment for adiposity. For artificially sweetened beverages the incidence rose by 8% per one serving/day. There was no risk increase for fruit juice.

Habitual consumption of sugar-sweetened drinks was associated with a greater incidence of type 2 diabetes, and was independent of adiposity.

Imamura F, O'Connor L, Ye Z, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. *BMJ* 2015; 351: h3576.

The consequences of banning trans fats

Trans fats are a type of unsaturated fatty acid. Although sometimes produced naturally, they are mostly found in processed foods to prolong shelf-life. However, trans fats increase the risk of mortality from coronary heart disease (CHD), especially among lower socio-economic groups where consumption of trans fats is highest. A recent study published in the BMJ examined the impact of different policies to ban or reduce trans fat consumption on deaths from CHD in England.

A total ban on trans fatty acids in processed foods might prevent or postpone 7200 deaths (2.6%) from CHD from 2015–20 and reduce inequality of mortality from CHD by 15%. Policies to improve labelling or remove trans fats from restaurants would be half as effective. A total ban would have the greatest net cost savings of about £264 million (US$415 million).

Regulatory policy to eliminate trans fatty acids from processed foods in England may reduce deaths from CHD and promote health equality.

Allen K, Pearson-Stuttard J, Hooton W, et al. Potential of trans fats policies to reduce socioeconomic inequalities in mortality from coronary heart disease in England: cost effectiveness modelling study. *BMJ* 2015; 351: 4583.

Interventions promoting hand hygiene

Hand hygiene among healthcare workers is possibly the most effective measure to reduce healthcare-associated infections, but compliance remains poor in many hospitals. In 2005, the World Health Organization (WHO) launched a campaign (WHO-5) to improve hand hygiene in healthcare settings by promoting five interventions. They included: system change, training and education, feedback and observation, reminders, and a hospital safety climate.

To quantify the efficacy of the campaign a systematic review and meta-analysis was conducted. There were considerable data to suggest that WHO-5 improved compliance significantly (odds ratio, 1.35) but could be further improved by goal setting, reward incentives, and accountability. The costs of interventions ranged from US$225-4600 per 100 bed days.

Promotion of the WHO-5 campaign is effective at increasing hand hygiene compliance among healthcare workers.

Luangasanatip N, Hongsuwan M, Limmathurotsaku D, et al. Comparative efficacy of interventions to promote hand hygiene in hospital: systematic review and network meta-analysis. *BMJ* 2015; 351: h3728.

Surgery

Hypothermia to increase kidney-graft function

After kidney transplantation, up to 50% of recipients experience delayed graft function (defined as the requirement for dialysis within 1 week of transplantation). Recently, a randomised trial has investigated whether mild hypothermia in organ donors before organ recovery reduced the rate of delayed graft function.

A total of 370 organ donors were enrolled into the study. They were then randomly assigned to either one of two targeted temperature ranges: 34–35°C (hypothermia) or 36.5–37.5°C (normothermia). The primary outcome was delayed graft function in the kidney recipients.

The study was terminated early due to overwhelming efficacy of hypothermia. Delayed graft function developed in 79 of the 285 kidney recipients in the hypothermia group (28%) compared with 112 out of 287 recipients in the normothermia group (39%). This yielded a significant odds ratio of 0.62.

Mild hypothermia in organ donors significantly reduced the rate of delayed graft function among recipients.

Niemann U, Feiner J, Swain S, et al. Therapeutic hypothermia in deceased organ donors and kidney-graft function. *NEJM* 2015; 373: 405–414.

Medical therapy for ureteric colic

Ureteric colic is caused by the smooth muscle contractions in the ureter in response to kidney stones. Most kidney stones will pass spontaneously within 4 weeks so ureteric colic is often managed conservatively. However, smooth muscle relaxant drugs such as tamsulosin and nifedipine may aid stone expulsion.

To test this hypothesis, a UK trial recruited over 1100 adults with confirmed ureteric colic. Participants were assigned to receive either tamsulosin (400 µg, (n=378), nifedipine (30 mg, (n=379), or placebo (n=379) to be taken daily for 4 weeks. The primary outcome measured the proportion of participants who did not need further intervention for stone clearance.

A total of 81% of the participants in the tamsulosin group satisfied the primary outcome compared with 80% in both the nifedipine and placebo groups – an insignificant difference.

Tamsulosin 400 µg and nifedipine 30 mg were not effective at decreasing the need for further interventions for kidney stone clearance.

Pickard R, Starr K, MacLennan G, et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. *Lancet* 2015; 386: 341–349.

Africa HEALTH CPD Challenge
See page 38 to test yourself on this article

Africa HEALTH CPD Challenge

Questions

Were you paying attention? Test your retentive capacities on issues raised in this edition of *Africa Health*. You can quietly test yourself, or – and we're particularly keen on this – you could make it a part of the foundation of a Journal Club in your department or health institution. Life-long learning is a collaborative exercise and the whole health team can be positively stimulated by being involved in such discussion.

Q1. *Plasmodium vivax* returns to Africa to threaten health

i) What is the complexity that *P. vivax* poses that *P. falciparum* doesn't; and what are the implications of this?

Q2. Supporting adherence to new malaria treatment with user-friendly materials

i) Name two of the three reasons revealed by a study (quoted in the article) of why patients had not completed their course of antimalarial tablets.

Q3. Clinical Review: Family Medicine

i) It is known that HIV positive patients may have an increased risk of cardiovascular disease and screening for such should be essential. But why might measuring blood pressure not be effective in identifying such disease?

ii) What was the somewhat surprising outcome about the perception of risk among a group studied in the Western Cape, South Africa? What are the implications?

Q4. Medicine: Diabetes and the gastrointestinal tract

i) In addition to diabetes, can you name four other causes for impaired gastric emptying?

ii) Name four causes of persistent diarrhoea in patients with diabetes.

Q5. Medicine: Gastroenterology in the elderly

i) In the UK (where the article was written) diverticular disease is common in the elderly. Sixty five per cent of all 65 year olds have it. But what percentage of these are asymptomatic?
   a) 45%
   b) 72%
   c) 83%

Q6. Medicine Digest

i) How did the ReEBOV new point of care Ebola test stand up in sensitivity and specificity terms to the gold standard PCR test?
   a) It was not as accurate
   b) Same accuracy
   c) It was more accurate

ii) Does maternal iron supplementation, benefit the mother, but leave the neonates at risk of infectious disease?

iii) Kidney stone conditions are usually managed conservatively in the hope that they will pass naturally within four weeks. But sometimes tamsulosin or nifedipine have been identified as being useful in reducing the pain and/or speeding the process or reducing the need for other interventions. Are they effective?

Answers

Answers continued on page 39

Q1. Once thought to be a more benign species, *P. vivax* is not seen for the dangers it brings in terms of morbidity and mortality in children, pregnant women and adults. Several major concerns include the fact that this species has a hibernating stage that makes subclinical, submicroscopic infection impossible, thus thwarting detection and elimination efforts. With most rapid tests seeking *P. falciparum* specifically, there is going to be an increasing need (if the trend continues) of tests with dual capability. This is going to be expensive to the campaign for the elimination of malaria.

Q2. 1) Many patients stopped their medication once they felt better; or 2) failed to complete the course because there were too many tablets; or 3) wanted to save some of the tablets for future episodes of malaria.

Q3. i) A study of young adults in Uganda found that hypertension was significantly associated with the older age-group, males sex and obesity, but there was a significantly lower prevalence of hypertension among participants with HIV. So identifying cardiovascular disease might need an alternative focus.

ii) The study group had no perception of risk. Things happen, or they don't happen. The implication is that the public health message needs to be altered from the usual 'don't do this or eat this' kind of approach. Or embark on education and orientation about risk.

Q4. i) Any from central nervous system disorders: demyelinating diseases, parkinsonism, brainstem vascular disease or neoplasia, acute physiological stress (e.g. intensive care state), spinal cord lesions including trauma, tumours and vascular disease. Autonomic neuropathies: DM, amyloidosis, paraneoplastic, primary autonomic neuropathy. Metabolic disturbance: Acute hyperglycaemia, hypokalaemia, hypothyroidism, porphyria. Drugs: opioids, anticholinergics, nicotine, levodopa, beta-adrenoceptor agonists. Infiltrative conditions: systemic sclerosis, amyloidosis. Other: post-gavotomy, post-operative ilius, radiation-induced, idiopathic pseudo-obstruction or myotonic dystrophy.

ii) Medications (e.g. metformin, acarbose, miglitol; rapid intestinal transit; bacterial overgrowth;

Answers

artificial sweeteners such as sorbitol and mannitol; coeliac disease; pancreatic insufficiency; or islet cell tumours.

Q5. Answer c) 83% (or specifically from the article between 80% and 85%.

Q6. i) Answer b) The same. Both tests had 100% sensitivity and 92% specificity.

ii) No. There was no added risk of infection (Plasmodium was the test in this case), but the iron supplements did significantly increase birthweight and also significantly increased maternal mean haemoglobin.

iii) No. In the study, there was insignificant differences between the two drugs mentioned and a placebo.Q1. Once thought to be a more benign species, *P. vivax* is not seen for the dangers it brings in terms of morbidity and mortality in children, pregnant women and adults. Several major concerns include the fact that this species has a hibernating stage that makes sub-clinical, submicroscopic infection impossible, thus thwarting detection and elimination efforts. With most rapid tests seeking *P. Falciparum* specifically, there is going to be an increasing need (if the trend continues) of tests with dual capability. This is going to be expensive to the campaign for the elimination of malaria.

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Out of breath (answers on page 33)

Part one

Daniel is a perfectly healthy and active child passing all his developmental milestones at the usual age. So it was a surprise to his doctors that his mum, who is doing her best on her own to bring him up along with his 3-year-old sister, brought him to see them because of sudden onset of shortness of breath and cough. There was no history of foreign object inhalation, and with a lack of obvious wheeze the clear diagnosis was made of bronchiolitis. Daniel was admitted, his symptoms eased rapidly with oxygen and observation only for three days, and he was discharged home apparently happy.

Q1 Which of the following possible diagnoses in an apparently otherwise healthy child with these symptoms is the most likely?

a) Bronchiolitis was the correct diagnosis to make in the circumstances.
b) Asthma may present for the first time in this way in a child of Daniel's age.
c) Inhalation of a foreign object is still at the top of the list, even without a history of it from mum.
d) Tuberculosis is always to be considered in unexplained dyspnoea, despite there being no obvious contact with other cases.

Part two

Q2 Eight days later, Daniel returned to the clinic with the same symptoms. This time he had a chest X-ray, which was reported as normal. This was considered to be a recurrence of the bronchiolitis, from which again he made a fast recovery with rest and oxygen alone. Which of the following statements are true?

a) You should now rule out bronchiolitis – it is very rarely a repeat illness.
b) The normal X-ray rules out an inhaled foreign body.
c) The resolution of symptoms with oxygen and rest alone also rules out foreign body inhalation, the signs and symptoms of which would gradually worsen.
d) Asthma is the most probable diagnosis even without obvious wheeze.

Part three

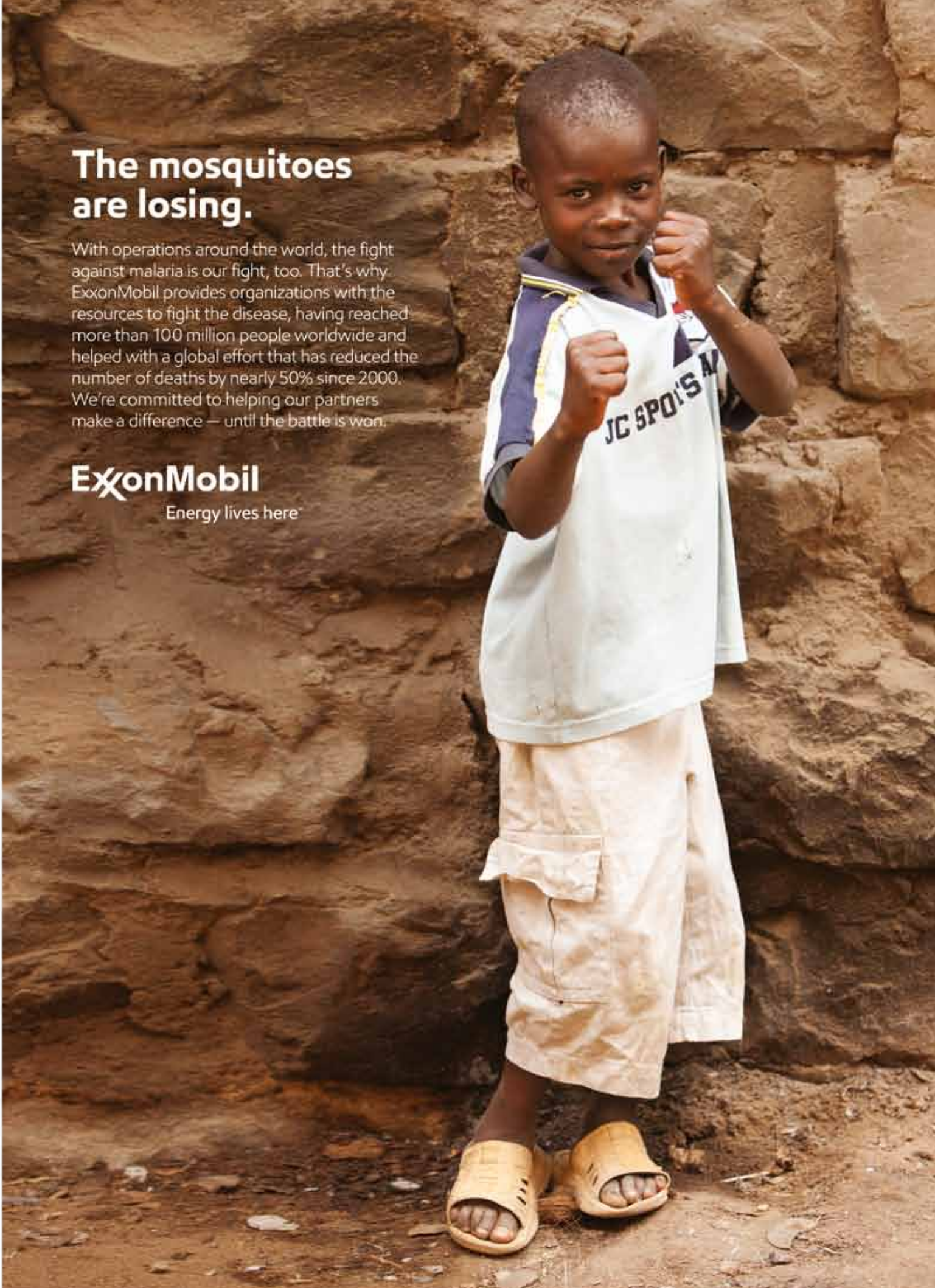
Q3 Daniel went home after three days apparently back to normal, and on no medication. He remained well for a month before being re-admitted, this time with a history for the previous three days of increasing cough, respiratory distress, and stridor. Now for the first time he had bilateral wheeze and rough upper airway sounds with each inhalation and exhalation. He was given nebulised salbutamol and adrenaline and he improved substantially, but the stridor remained. A repeat chest X-ray was normal, but he was still ill enough to be admitted. Which of the following was the next step in his treatment?

a) The appropriate antibiotic for his severe bacterial upper respiratory tract infection.
b) Steroids for his repeated asthma.
c) Naso-endoscopic inspection of his epiglottis and larynx.
d) Full examination of the respiratory tract in theatre by a paediatric ENT specialist.
e) Rest and oxygen therapy as before to allow the repeated viral infection to resolve.

Part four

Q4 What are the risks for Daniel if this condition were to be left without intrusive investigation and treatment?

a) Very few. His chest will slowly recover on rest and inhalers.
b) Sudden asphyxia and death.
c) Pneumonia.
d) Atelectasis.
e) Haemoptysis.
f) Bouts of high fever.


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