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Addresses

Prof. James Ware
Editor-In-Chief,
Department of Medical Education and Postgraduate Studies, The Saudi Commission for Health Specialties, P.O.Box 94656, Riyadh-11614, Saudi Arabia
E-mail: editor.jhs@scfhs.org
Websites: http://www.thejhs.org
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Tuberculosis (TB) is an ancient disease because evidence of its presence has been found in the spines of thousands-of-years-old Egyptian mummies, as well as in the people of both ancient Greece and Imperial Rome. When the bone and soft tissue samples from 85 ancient Egyptian mummies were obtained from different tomb complexes in Upper Egypt and analyzed for the presence of ancient \textit{Mycobacterium tuberculosis} (MTB) complex DNA (aDNA) and further characterized by spoligotyping (a PCR-based technique), it was confirmed that an even higher frequency of this disease was present in the ancient population.\cite{1} This disease gained the name of the white plague because 100\% of the population was infected resulting in 25\% of all deaths in Europe during the 17\textsuperscript{th} and 18\textsuperscript{th} centuries. In 1882, Robert Koch confirmed the infectious character of the disease by discovering the bacteria, \textit{Mycocabacterium} using a newly developed methylene blue stain. Streptomycin was the first antibiotic isolated in 1943 by Albert Schaftz in the laboratory of Selman Abraham Waksman at Rutgers University and the first widely accepted randomized curative trial was carried out in 1946-1947.\cite{2}

With the advances of science, especially medical science, many research studies have been done on each and every aspects of the disease such as the causative organism, diagnosis, treatment, prevention and development of vaccines. In 1993, the World Health Organization (WHO) declared TB a public health emergency, and in response to which efforts to improve TB care and control intensified. In 1999, WHO developed the DOTS strategy comprising five elements including political commitment with increased and sustained financing, case detection through quality-assured bacteriology, standardised treatment with supervision and patient support, and an effective drug supply and standardised system of recording and reporting the number of cases detected and outcomes of treatment. WHO's current approach to care and control the disease is the Stop TB Strategy which was launched in 2006 with the goal of dramatically reducing the global burden of TB by 2015, and achieving universal access to high quality care for all people with TB, protection of vulnerable populations and reduction of the socioeconomic burden associated with TB. Despite these global scientific and societal efforts, TB is still posing a significant threat to human populations. According to the latest estimates by WHO, in 2011, 8.7 million people fell ill with this disease and 1.4 million died from the disease.\cite{3} Furthermore, the bacille Calmette-Guérin (BCG) vaccine, developed in 1921, is now widely used in developing countries to immunize infants against TB, although it is only partially effective. Therefore, there is a great need to develop a booster vaccine for BCG or a new effective vaccine with 100\% efficacy.

Today, global TB control is facing major challenges. Firstly, the syndemic interaction between the human immunodeficiency virus (HIV) and TB epidemics has deadly consequences, especially in Africa, where the prevalence of HIV infection is high, and co-infection with MTB has reached 79\%. In 2011, about 430,000 people died of HIV-associated TB, and almost 25\% of deaths among people with HIV are due to TB. In the same year, there were an estimated 1.1 million new cases of HIV-positive TB, 79\% of who were living in Africa. Secondly, another critical issue is drug resistant TB including both multidrug-drug resistance (MDR) which fails to respond to standard first line drugs and extensively drug-resistance (XDR) which fails to respond to both first-line and second-line drugs. The MDR-TB is treatable using second-line drugs, but drugs
in the second line are limited and their availability is not guaranteed in many places in the world. For XDR-TB there are only a few effective drugs available but accessibility to these drugs is again a problem. In any of the types of drug-resistant TB, the length of the treatment is longer than usual; the cost is higher and can produce severe adverse drug reactions in patients. In 2011, there were about 310,000 cases of MDR-TB among reported cases with pulmonary TB around the world. Almost 60% of these cases were in India, China and the Russian Federation. It is estimated that about 9% of MDR-TB cases had XDR-TB.\[3\]

Now, the WHO has set an important goal of eliminating TB by 2050 described as “Millennium Developmental Goal of Eliminating TB by 2050”.\[4\] The first target in achieving this goal is to reduce the prevalence and deaths due to TB by 2015 to 50% compared with the baseline of 1990. If at the end of 2013, we are still reporting several million people falling ill due to TB, it means that there are several critical gaps present in the global TB control efforts. Although the WHO seems to be very efficient in providing support and leadership to control TB, these challenges need to be addressed by national TB programmes with focused attention and tailored approaches. The goal of eliminating TB by 2050 depends on the development of new diagnostic tools, drugs and vaccines. We hope that the WHO, researchers and governments will work in close collaboration with each other to develop new diagnostic tests for both drug-resistant and drug-susceptible TB, better and shorter treatment for all forms of TB and vaccines more effective than BCG.

**REFERENCES**

I love this point in our world conference. On the first day, we all tend to sit with people from our own countries. Then the WONCA magic happens. We meet colleagues from around the world, share ideas and challenges and become friends. And we mix up. Look either side of you now. Chances are that the people sitting on either side of you are now your friends from other parts of the world.

Thanks to the president, Svatopluk Byma, and all the members and staff of our host, the Czech Society of General Practice, for a wonderful conference and for your warm hospitality. My special thanks to Bohumil Seifert, as chair of the conference organizing committee, and to Vaclav Benes as chair of the scientific committee and to all those who have worked with you both on making this such a successful event.

Thanks to everybody here for being so active in the conference programme and sharing your ideas and innovations and challenging each other to think deep and wide. I hope you have made many new friends and will return home inspired about the work that we do as family doctors.

And thanks to all the young doctors who attended this meeting and inspired us with your passion for family medicine and global health. The Vasco da Gama Movement, the European young family doctor group, has run a wonderful programme over the past week. And here in Prague, a new group has been established for young family doctors in Africa, led by Kayode Alao from Nigeria.

Together we strengthen family medicine across the world to the benefit of our patients, our communities and humanity. During this presentation I will share with you some images of our colleagues in Indonesia working in some of the family medicine clinics I visited there last month. They have agreed to share their images with you. The patients you see in these images are other family doctor colleagues role playing so that we do not breach patient confidentiality.

I also need to begin with a word about words. When I say family doctor, I mean you. Whether you call yourself a general practitioner, a GP or a family physician or a primary care doctor. Whatever you call yourself, and whatever your patients call you, when I say family doctor I mean you, my sisters and my brothers in family medicine. The language we use to describe who we are, does not matter. What matters is the common work that we do, the vision that we share and the outcomes that we achieve.

I am going to speak about WONCA, our world organization of family medicine, and the challenges ahead for family medicine around the world.

This week I asked some young Czech family doctors who is the most famous Czech person ever. If you are from the English-speaking world, like me, it might be Good King Wenceslaus, St Vaclav if you are Czech. Or if you love literature it might be Frank Kafka, or if you love music, Antonin Dvorak. When I asked my taxi driver coming here from the airport he assured me the most famous Czech person is Martina Navratilova.

The name I was seeking is my Czech hero — this man, Vaclav Havel, the first president of the Czech Republic, a playwright as well as a global political figure and a voice for world peace. Vaclav Havel once wrote, “The salvation of this human world lies nowhere else than in the human heart, in the human power to reflect, in human meekness and human responsibility”.

I think this is a wonderful message for family doctors with our combination of compassion and intellect and humility and responsibility, we have within us the power to do great good, to make a real difference in
WONCA allows us to come together to work together to make this a reality.

In the words of our very first WONCA president, Dr Monty Kent Hughes, speaking to the first WONCA world council in 1972: “The future of our professional discipline will depend on our ability to work together in the service of humanity”.

WONCA is the global voice of family medicine. We are also the eyes and ears of global healthcare observing and listening to our individual patients and our communities and identifying their healthcare needs. And we are the head and heart of global medicine — combining our scientific knowledge as medical practitioners with tender loving care. Indeed this is the Latin motto of several of the member organisations of WONCA: *Cum scientia caritas* — ‘with scientific knowledge and tender loving care’.

WONCA represents you and your professional college or society at a global level. WONCA advocates for the important work you do every day in meeting the healthcare needs of your patients and your communities.

Why do we do this? Because family medicine is important.

Because the evidence is clear that health systems based on strong primary care, which includes strong family medicine, are the most efficient, equitable and cost-effective.

Because strong family medicine is the best way to improve the health of individuals, families and communities.

Because every family should have a family doctor who the members of each family can trust for their medical care and advice.

Because family doctors are part of the social fabric of our societies and we work to keep the fabric of healthcare together.

The family doctor has an important role to play in the life of every family in every community in every nation of the world.

WONCA, like me, was born in Melbourne many years ago. It started with a small group of family medicine colleges and academies that banded together to create a world body, which shared an ideal of training and education for family medicine and high standards for clinical care in all nations of the world.

WONCA now has 118 Member Organisations representing over 400,000 family doctors in over 130 countries and territories around the world. As I mentioned on Thursday, the 400,000 family doctors represented by WONCA, and including all those of us here, each year have over 2 billion consultations with our patients. Two billion. That’s the scope of our current work and our influence.

But we need to do more. We need to work to ensure that every family doctor, every GP, every primary care doctor, joins us in our commitment to deliver high quality primary care to our patients and communities. And we need to expand our commitment to the education and training of family doctors and quality care and primary care research to the 80 nations of the world where WONCA does not yet have a presence.

WONCA calls for a family doctor for every family. This means that every family has access to a caring committed family doctor working with other primary healthcare providers, including dedicated nurses and midwives and community health workers, to provide comprehensive continuing care to all people.

And by family I mean family in its broadest context. Not just families with a mum and a dad and 2.3 kids and a dog. We provide care for every member of every family in the global family. As family doctors, we do not discriminate. We care for all families — nuclear families, extended families, rich families, poor families, gay families, sad families and families of just one person.

The beauty of family medicine is that we put the patient in the centre of care and have a focus on the whole person, rather than on individual diseases.

In the words of Ian McWhinney, one of the giants of our profession who passed away last year, “The family doctor is committed to the person rather than to a particular body of knowledge, group of diseases, or special technique”.

Ian also advised us that, “ideally, family doctors should share the same habitat as their patients”. This allows us to best understand the social context of our patients’ lives.

While our clinics may be different from country to country, what is important is the way we are the same — through our commitment to comprehensive, continuing, coordinated whole person care. Through care that is person-centred, and family and community-oriented. Through first-contact care, acute care, chronic disease management, prevention and health promotion. And through our understanding of the interplay between
population health and the health of individuals in our communities.

Karen Kinder has reminded us about the wonderful legacy of Barbara Starfield, and how Barbara, through her research, provided us with the evidence of the benefits of primary care in lowering the cost of care, improving access to services and reducing the inequities in a population’s health.

I last met with Barbara a few months before she died in 2011. Barbara was keen to talk about the biggest challenges she saw for family medicine in the future, and what WONCA, and what Michael Kidd as your incoming president, should be doing. I wrote it all down and here is Barbara’s last message for WONCA:

“Here are the three challenges I think you should focus on:

How do we develop primary care research to address the challenges of care for people with comorbidities?

How do we truly adopt patient-centredness into family medicine?

How do we use the information from primary care to improve population health?”

There is enough in that simple statement for a dozen PhDs in family medicine. Barbara recognised the failure of guidelines to accommodate co-morbidity and multi-morbidity and the need to turn our evidence-base upside down.

Barbara recognised that primary care is person-focused, rather than disease-focused and that our health systems need to be reformed to focus on person-centred care and to embrace our greatest allies in family medicine — our patients.

And Barbara recognised the power of the information that we are starting to collect through digital means in primary care and how this can be used to improve population health? We need to build our own evidence base from primary care. And where do we get this evidence from? The answer is right in front of us. It is from our encounters with our patients. In the words of immediate past WONCA president, Rich Roberts, “If we want evidence-base practice, we need practice-based evidence”.

Research like this is critical to family medicine. We all appreciate that research is a core component of family medicine training, scholarship and clinical practice in all our nations. WONCA brings together some wonderful primary care researchers who put their heads together to provide solutions to some of the world’s greatest health challenges. This week, WONCA’s working party on research, led by Waris Qidwai from Pakistan, has drafted an excellent statement on the importance of research and research training in family medicine.

The potential of e-health, especially the aggregation of patient data from electronic medical records, is extraordinary. It will assist us in identifying the healthcare needs of populations and highlight those areas where we can work together to make improvements.

In the words of Sir Muir Gray, Chief Knowledge Officer for the National Health Service in the United Kingdom, “In the 19th century we needed clear clean water. In the 21st century, we need clear clean information”.

The paramount responsibility of WONCA, and of each of our member organisations, is to our patients and our communities. Family doctors, no matter where we work, ensure that health is affordable, safe, appropriate and equitable.

At a time of rapid change and social unrest and conflict in many parts of our world, family medicine provides comfort to our patients, our communities and our nations.

We can provide comfort because we are used to dealing with complexity and uncertainty.

We provide comfort at a time when uncertainty is increasing for our patients who are faced with a barrage of choices and options and a wealth of misinformation thanks to the Internet.

We provide comfort to our nations, which are facing uncertainty about their capacity to provide healthcare to all people and know that they should be keeping people out of expensive hospitals, but are not sure how to do this.

At this time of uncertainty about the future of healthcare, the role of the family doctor continues to grow. And this need for comfort moves our global organization into an increasingly strategic role with the World Health Organization (WHO) and other global health organisations.

We can take on this role because we are familiar. People know who we are and what we do. Family doctors have been around for a long time.

The first family doctor to record his thoughts about medical practice and medical education was Hippocrates.
We now recognise that Hippocrates was a genuine family doctor, sitting under a plane tree, seeing patients of all ages, treating all conditions, providing first point of contact as well as continuing and comprehensive care and recognising the links between the physical, psychological, social and spiritual influences on his patients’ health and well-being.

Few of us get to practise medicine nowadays sitting under a plane tree, like Hippocrates, although you can still sit under the descendent of his tree on the Island of Cos. One of the things that unites us as family doctors is our differences. Each country has developed a system of primary care to meet the needs of its own population — as village healers, as apothecaries, as state funded community health providers, as country doctors, as hospital based primary care providers, as community-based family physicians, as general practitioners, as gatekeepers to the rest of the healthcare system.

I believe this is the beginning of a new Golden Age for family medicine. This is a painting of the Golden Age by Lucas Carnach the Elder; perhaps you can see yourself here. In countries all around the world, the message is getting through about the importance of strong primary care and the role of family doctors in ensuring universal access to healthcare and equitable healthcare outcomes.

You know the many healthcare challenges our world is facing. It is becoming increasingly apparent that our generalist tradition of primary care is the only way that nations will be able to effectively tackle the diverse health challenges facing the people of our world. Indeed Dr Margaret Chan, the Director-General of the WHO spoke earlier this week about the renewed focus of the WHO and all its activities on primary care and family medicine.

Primary care is the key to the control of major communicable diseases — dreaded diseases like HIV, tuberculosis and malaria, and new and emerging diseases like SARS and new strains of influenza and other viruses. This is a remarkable time in human history with the ability to turn pandemics of infectious diseases like HIV, into controllable low-level endemic diseases but this will only happen through engagement with strong primary care.

Primary care is the only way we will be able to effectively address the rapidly rising burden of mental health problems across the world.

Primary care is the only way nations will be able to effectively manage the healthcare needs of the increasing proportion of elderly people.

Primary care in the only way we will be able to effectively contain rising healthcare costs in our nations, through support for preventive care, health promotion and improvements in chronic disease management and the management of co-morbidities.

And primary care is the only way we will be able to meet the challenge of rising consumer expectations fuelled by the Internet.

If we are going to have strong primary care in each of our nations then we need strong family medicine. If we are going to effectively tackle these major healthcare challenges, then our academies and colleges need to join together and share our knowledge and resources. This is a major role for WONCA. Bringing our member organisations together to share our knowledge and our experience to benefit the people in each of our nations.

As family doctors we are all specialists, whether or not our governments provide us with specialist recognition.

We are specialists in primary medical care and in the generalist tradition of medical practice.

We are specialists in preventive care and health promotion; in early diagnosis and management; in the management of undifferentiated illness, acute conditions, medical emergencies, and people with complex chronic diseases and multiple morbidities; in the management of mental health challenges and the impact of social and environmental issues on health; in palliative care and the ways to support our patients to die with dignity. And each of us is a specialist in the unique healthcare needs and concerns of our own unique patient populations. We are all specialists. Do not let anyone tell you otherwise.

To support our important work we need strong standards for clinical care and standards for education and training and we need strong government and community support.

Governments need to value our generalist traditions. Workforce arrangements need to support the generalist approach to high quality primary medical care.
What percentage of our medical graduates do we need to train in each country in the specialty of family medicine? If we are to meet the true health needs of our communities, in most of our countries it is likely to be at least 50% and probably more. You might like to reflect on the current percentage in your own country. Many nations continue to train large numbers of consultant specialists and sub-specialists way beyond their nation's needs. We need more family doctors because we provide our health systems with a healthy dose of common sense. We can say, 'What, really, we need 20% of our medical school graduates training to be cardiologists? I don't think so'.

We also have an unbalanced distribution of our family doctor workforce around the world. What role can WONCA play in addressing the redistribution of our global workforce? How do we support family doctors who would like to spend part of their career working in other countries? How do we support and encourage family doctors to spend part of their career working in rural and remote locations? How do we support and encourage family doctors to spend part of their careers working with disadvantaged and vulnerable communities?

Should WONCA take on a role similar to Médecins Sans Frontières, Doctors Without Borders, not providing doctors to work in conflict zones, but providing skilled family doctors to work in areas of medical workforce crisis?

So why do I say that this is the start of a worldwide golden age for family medicine?

Well it is because in 2008 something extraordinary happened. The world re-discovered the importance of primary healthcare and the role of the people working providing primary care services to their local communities. Now I know that you probably did not realise that we needed to be re-discovered. After all we have been doing the work we had been doing for a very long time.

But in 2008, the World Health Report from the WHO was devoted to the reinvigoration of primary healthcare.

The following year, at the Annual World Health Assembly of the WHO, a resolution was passed committing all the member nations to reinvigoration of their primary healthcare systems. This included recognition of the important roles of the members of each nation's primary care workforce including mentioning, for the first time in a WHO resolution, the role of family doctors. Yes!

And on Tuesday this week, here in Prague, Dr Margaret Chan delivered her historic speech about the rising importance of family medicine.

A focus on primary healthcare by the WHO is nothing new. The 1978 Declaration of Alma Ata committed the nations of the world to strive to attain 'Health for all by the year 2000' and recognised that strong 'primary health care is the key to attaining this target'.

However, the world failed to achieve health for all people by the Year 2000.

As a consequence, in 2000, the United Nations agreed to the Millennium Development Goals (MDGs); eight goals with targets to be reached by 2015, eight goals ‘to free people from extreme poverty and multiple deprivations’.

Sadly progress in the health-related MDGs, numbers 4, 5 and 6, are not as significant as we would like to see but we have seen millions of lives saved through reductions in preventable deaths.

Part of the problem with the MDGs is in their implementation. Often initiatives to support the MDGs in a country fail to engage with the existing primary care workforce.

This week I discussed with Dr Chan the challenges of meeting the polio eradication targets and how our members in Pakistan had commented on a lack of engagement with many of the family doctors and other primary care workers in the remaining endemic areas; doctors with the trust of the local populations who may be able to be part of assisting in the final moves towards global eradication.

The MDGs have also come in for some criticism because of what they are missing. They do not tackle the need to strengthen primary care, or to tackle chronic disease and mental health, or to address the social determinants of health, or to ensure universal coverage for people in both rural and urban areas.

The global policy pendulum is now swinging back to a focus on universal coverage. And for good reasons.

Universal health coverage has been part of the charter of the United Nations since 1948. And universal coverage does not mean meeting the needs of 80% of the population — it means ensuring that healthcare is available to everybody.

People-centred care is a core component of universal health coverage, and there will be an increasing role
for family medicine over the coming few years in many countries to ensure this happens.

As Dr Chan advised us on Tuesday, the United Nations is now starting the discussions about its focus following 2015 — the post-MDG era. Above the clamour of thousands of interest groups and self-interested industries, WONCA needs to ensure the clear voice of family medicine on behalf of our patients and communities is heard during these debates.

We need to be clear about our role in increasing life expectancy and achieving equitable outcomes.

And we need to support the focus on the social determinants of health and how we ensure marginalised populations are not excluded from healthcare.

Indeed, how do we support the de-marginalisation of marginalised populations, those groups of people in our communities most at risk of poor health?

How do we meet the challenge of meeting the health and well-being needs of the many diverse communities around the world? We do so by continuing to adapt to changing health needs and expectations.

Fortunately one of the greatest strengths of the people working in family medicine is our diversity, our community leadership, our resilience and our unwavering commitment to our patients and our communities. These are qualities that we need to reinforce and cherish.

These are some of my family medicine colleagues in central Australia, in Alice Springs. This week, in a historic move, WONCA has established a new working party on health issues for Indigenous people and minority groups, led by Tane Taylor from New Zealand.

This is the chart of life expectancy in the nations of the world — as you can see there is significant disparity in life expectancy based on the accident of where you are born. A difference of more than half a century, two and a half times the life expectancy for one over the other, all based on the accident of where a child happens to be born. It’s 2013. We have to do better.

Family medicine, as a component of primary care, has the power to play a transformative role in the shaping of societies. We have the power to tackle this disparity and transform the world we live in but we have got a lot to do.

There are 7 billion people on this planet. The WHO tells us that 1 billion have no access to any healthcare services.

In the words of equal justice advocate, Bryan Stevenson, in an inspiring presentation on TED:

“You judge the character of a society, not by how they treat the rich and the powerful and the privileged, but by how they treat the poor, the condemned, the incarcerated”.

This is one of the challenges for 21st century family medicine. How do we prepare our young doctors and our medical students to tackle these challenges of health inequity, of inequity of access to healthcare, of inequity of outcomes of healthcare and ensure our health systems are socially accountable?

And how do we work together to ensure that high quality healthcare is available to all people in every nation of the world?

There are those who say that family medicine has no real role to play in low and middle-income countries. Well we have blown that theory out of the water. The new edition of the WONCA guidebook includes the chapter from the WHO showcasing the research into the impact family medicine is having in improving health outcomes in many middle-income nations including Brazil, China, Thailand and countries of the Eastern Mediterranean region. And there is a chapter outlining the remarkable work that is underway across Africa to strengthen family medicine, especially involving WONCA member organisations within Africa supporting developments in neighbouring nations.

What these development demonstrate is the need to strengthen the whole healthcare workforce, including family doctors, community nurses, community health workers and traditional birthing assistants, and support working together to deliver appropriate care to all people. People in low-income countries still want and deserve access to healthcare, access to caring clinicians, access to life saving medications.

We also need to embrace the concept of reverse innovation. What can health systems in high-income countries learn from the health systems in lower income countries? It is something that each of who spends time working in another health system in another country learns very quickly.

It is also a lesson which was emphasised by another of our past WONCA presidents, Rajakumar from Malaysia who wrote that: “Experience in different health systems will make us better doctors and better human beings”.

It reminds me also of the wise words of past WONCA president, Dr Michael Boland from Ireland, who
addressed the World Health Forum in 1995 on the question of what do people expect from their doctors. Michael said that people expect: A doctor who will listen, A doctor who is flexible, A doctor who will help sort out problems and A doctor who will be there when I need her/him.

Dr Margaret Chan, in her meeting with the WONCA executive last year, spoke about the world’s post-2015 development agenda because development means economic growth, and health is a pre-condition to economic development.

But Dr Chan has also recognised that primary care is not cheap and must not be a ‘B-team’ version of healthcare delivery.

But in order to provide universal coverage, we need to stem the costs of healthcare, and can do so through increasing our investment in community-based health services, and reducing the amount spent on hospitals. And at the same time there must be a movement of funding from hospitals to the community, rather than expecting more community-based care to be delivered with no increase in resources.

We need to work with our global partners, the WHO, the World Bank and others to bring high quality primary care to the 1 billion people on this planet who currently have no access to any healthcare at all.

The same model of care is not going to work for each community, which is why family medicine is so important. We adapt to our community needs.

I want to share some thoughts on what drives doctors to work with marginalised communities. Some of the focus of my own research team’s recent activity has been on the pathways followed by family doctors who work with marginalised communities and what family doctors describe as motivating their initial engagement. These are interest and inspiration, community calling and being in the right place at the right time. The perceived rewards that support and sustain our continuing engagement include the motivation presented by the challenges, feeling that we are able to make a difference and enhanced professional identity as a result of our meaningful work.

I have learned many things about family doctors as I have the opportunity to visit many of your countries and watch you at work. As family doctors, we all recognise that no one is perfect. We all have our flaws. We all make mistakes. This is part of being human. And because we have a deep understanding as family doctors about what it is to be human, we tend to be less judgmental than many of our peers. We do not tolerate stigma and discrimination. We accept people for who they are and we get on with our important work.

Many of our countries are responding to the global impact of health system reform that is shaking up the delivery of primary medical care around the world and this brings about challenges for the training of family doctors. Many countries have large numbers of general doctors who have received no post-graduate training but who wish to be recognised as specialist family doctors. We need to embrace all our colleagues in primary care. We need to find innovative ways that work in each of our countries to up-skill and support the professional development of our peers. We cannot afford to disregard the contributions of all doctors working in primary care.

At the same time we need to develop greater clarity around how we educate our future family medicine workforce to ensure we meet the future healthcare needs of the people of our nation.

We need to better support our GP trainers and teaching practices and provide incentives and motivation for those who do not teach at present to join us. After all, teaching the next generation is a fundamental responsibility of each medical professional as part of our Hippocratic tradition.

It is clear that there are challenges to the enhanced apprenticeship model of family doctor training that has served many of our nations well, yet by its very nature the apprentice ends up cast in the mould of the master. It is a confronting reality for today’s family doctors that tomorrow’s family doctors may look quite different to what we have all been used to. Family medicine trainers need the flexibility to train the next generation for some quite different roles. Family medicine training must allow our registrars to develop into what they need to be to best meet the future healthcare needs of their patients and their communities.

And the training we provide to our family medicine trainees must be based in primary care. Effective training for family medicine does not take place on the medical and surgical wards of hospitals. Our trainees
are not fodder to carry out the menial tasks of other specialists. The training of our future family doctors needs to be based in our communities working as members of primary care teams.

These challenges are nothing new. Family medicine and family medicine training is always changing, although many of the fundamental underlying principles remain the same. WONCA’s education working party, led by Allyn Walsh from Canada, has this week released our new global standards for family medicine education, and I commend them to you.

This could also allow for more contemporary competencies to be added to the family doctor’s traditional skill set, for example skills in management, teaching, research, quality and safety, teamwork, e-health, leadership, personal resilience and personalised medicine. Better horizontal links must be established with other craft groups to strengthen inter-professional learning as family medicine moves increasingly more to team-based care to better meet the complex needs of many of our patients and our communities. The WONCA working party on quality and safety, led by Daniel Thuraiappah from Malaysia, has this week drafted a statement, The Prague Statement, on the contemporary competencies in quality and safety in family medicine. It is an excellent document, which we will share with you over coming months for your comments via the WONCA website.

We need to be flexible and acknowledge that there are multiple ways in which each new doctor can acquire the competencies required for safe, independent and appropriate family medicine.

And do not underestimate the opportunities for our medical students and family medicine trainees to make a difference to healthcare and to outcomes while they are students and trainees. The key is to give our learners enough space to be the amazing creative individuals they are.

The digital world also provides a lot of challenges. In our asynchronous world, how do we achieve continuity of care? But it will also bring benefits. We are starting to learn how tele-consultations can allow us to conduct home visits with our patients from a distance — we know the best way to understand our patients is through visiting them in their homes.

We need to embrace the opportunities provided by new technology. This is nothing to be afraid of. We are experts at adopting innovations into our practice and acting as translation agents for new technology. We are used to working quickly. We are used to change. We can accommodate innovation quickly when we see a direct benefit to the care of our patients.

Connectedness is important. We need to find ways to engage everyone in our global family. This week we launched WONCA’s new social media platform. I invite you to join me, through the WONCA website, on Twitter, Facebook and LinkedIn and discover new ways that we can work together to achieve our goals. Details are on our website: www.globalfamilydoctor.com

Something our chair, Iona Heath from the United Kingdom, said a few years ago really struck a chord with me, “I believe that general practice/family medicine is a force for good throughout the world”.

I am impressed with the commitment of family doctors to human rights issues. I am convinced that family doctors care about human rights. The basic expectations we all have about how we and our families and all people should be treated.

As family doctors we have social responsibilities. Each of us needs to be an advocate for social justice and human rights.

We need to stand up for freedom and justice and peace. Nearly 1.5 billion people live in countries affected by violent conflict with the associated terrible immediate and longer-term health outcomes.

We need to speak out for what is right, to say ‘this is not OK’, and in so doing contribute to social change.

We need to contribute towards ensuring equity of access to healthcare — ‘a fair go for everyone’.

And we need to care for the health of our planet as well as the health of our patients. What is good for the climate is also good for our patient’s health — reducing obesity, increasing physical activity and healthy improvements in diet.

After all if we, as family doctors, with our privileged position in society, and our access to pretty much the entire population in our communities, do not stand up for these things, who will?

Are you familiar with the term ‘a fair go’? It is an Australian expression meaning that we treat everyone equally. I want to be known as the WONCA president who called for a fair go for every person in this world.

And we have a great opportunity to do all this. We see the consequences of social inequality on the health of our patients and our communities. In the words of the
German pathologist, Rudolf Virchow, who worked not far from here, doctors “are the natural attorneys of the poor, and social problems fall to a large extent within their jurisdiction”. These days this role falls to the family doctor. We understand the social determinants of health.

As family doctors we all work hard. I know that many of you work under very difficult conditions, that the resources that you need to do your job are often not available, that the hours you work and the demands on your time can be arduous, that your resilience is tested regularly. And we often feel unappreciated. And do not often hear the words thank you. It is why WONCA has established World Family Doctor Day, held on May 19 each year, to acknowledge the important work that we do.

So today, on behalf of the 2 billion people around the world who benefited from your care and support over the past year I say thank you. Thank you for your commitment to being a great family doctor.

And always remember, no matter what our governments do, our important work as family doctors will continue.

Never forget that we are privileged to work in family medicine and to work with our local communities. We are here to stay.

And never forget that through our work each of us makes a positive difference in the lives of our patients and our communities every single day.
Fast-track surgery: A new concept of perioperative management of surgical patients

Gabriel Rodrigues, Chandini Ravi, Raghunath Prabhu
Department of General Surgery, Kasturba Medical College, Manipal University, Manipal, Karnataka, India

ABSTRACT
In the past few decades, surgery has advanced greatly because of an improved understanding of perioperative pathophysiology, development of minimally invasive operative techniques and advanced anaesthetic techniques. Fewer operations are requiring extended periods of hospital stay and a growing number of procedures are performed on an ambulatory basis. The pressure on medical systems is continuously growing as a result of economic constraints, increasing numbers of patients undergoing surgical procedures and greater patient autonomy. Patient awareness is steadily increasing along with their participation in their own care, leading to expectations of a higher standard of care. This has led to the development of a new concept of fast-track surgery.

Keywords: Anaesthesia, hospital stay, perioperative, recovery, surgery

INTRODUCTION
Surgery initiates a complex stress response comprising of metabolic, neuroendocrine and inflammatory changes, which result in the activation of sympathetic system and a catabolic state. These physiological stress responses due to major surgery frequently lead to pain, nausea, ileus, impaired pulmonary function and increased cardiac demands. These sequelae lead to delayed postoperative recovery.[1] Enhanced postoperative recovery is measured by the length of hospital stay, morbidity and mortality, length of time taken for complete recovery and patient satisfaction. Fast-track surgery programmes employ a combination of evidence-based strategies to expedite recovery following surgery. These strategies have developed over time and we now have better surgical techniques, anaesthesia and modalities of pain control and rehabilitation at our disposal.[2] The combination of these approaches aims to reduce the perioperative stress response and organ dysfunction, the incidence of postoperative complications and the cost and duration of hospital stay required.

The principle of fast-track surgery has been applied to a variety of procedures so far including abdominal, gynaecological, orthopaedic and cardiothoracic surgeries, reflecting the growing interest in this concept. While elective abdominal surgery patients are the main focus of fast-track surgery programmes, the same principle may be applied to the management of all surgical patients. Table 1 provides a comparison of the duration of hospital stay in fast-track surgical programmes as compared with their conventional counterparts.

This article reviews the core principles employed by fast-track surgery programmes based on evidence available in literature for each component of perioperative care in order to incorporate these components into a multi-modal programme for enhanced postoperative recovery.

Patient care strategies
The fast-track concept should be incorporated into all phases of perioperative care by implementing evidence-based preoperative, intraoperative and postoperative strategies, thus forming an integrated
surgical management model in order to optimise patient outcomes [Table 2].\textsuperscript{26,27}

**Preoperative strategies**

*Patient selection and assessment*

Postoperative organ dysfunction is related to preoperative co-morbidities in the patient.\textsuperscript{11} Existing co-morbidities must be assessed for an estimation of surgical risk and optimisation of organ function. The continuation of medicines the patient is already taking, especially β blockers\textsuperscript{28} and other medications that blunt catecholamine release must be reinforced, as discontinuing such medications preoperatively may contribute to increased surgical stress and continuing them up to and after surgery has been shown to reduce complications.\textsuperscript{29} The surgical team should identify patients suitable for the fast-track approach, as patient participation is required for accelerated recovery.

Patient education is an integral factor contributing to the success of any fast-track programme. The patients must be provided clear, concise and adequate information regarding the procedure they are about to undergo, as it reduces their anxiety. In addition, a realistic picture of their postoperative period and the recovery process must be provided. Educating the patient also provides a platform of two-way communication between the care provider and the patient whereby the concerns and queries of the patient are addressed, reassurance is provided and their co-operation is gained. It places the patients in their rightful place as a partner in their medical care where they can make well informed decisions, giving rise to increased satisfaction, fewer complaints and therefore better overall outcomes. When sufficient information is not provided by the healthcare providers, patients tend to gather information from other sources such as other patients and the internet, which may not provide an accurate picture and would give rise to gaps in their understanding of the planned surgery. In addition, patient education in the perioperative period has been shown to reduce the need for pain relief by reducing anxiety.\textsuperscript{30} Counselling is therefore a necessary component and it is recommended that it be provided pre-admission.

Patient nutrition must be optimised prior to surgery as patient undernutrition impairs the immunological response, leading to impaired wound healing and increased morbidity and mortality. Those at risk for undernutrition must be identified such as malnourished or cancer patients, in who extended fasting may exaggerate the surgical stress response. The classical overnight preoperative fasting is one of the prime contributors to perioperative undernutrition. While the required fasting period for major surgery is usually around 6 hours, in reality the overnight fast tends to be a few hours longer. This prolonged fasting period results in dehydration and increased risk of aspiration as it reduces gastric emptying, increases the acidity of the gastric content and results in increased volume. Dehydration has been shown to be related to postoperative nausea and vomiting (PONV).\textsuperscript{11}

The fasting period aside, improper and inadequate nutrition is often the case in many hospital admissions. The traditional mechanical bowel preparation has been shown to be unnecessary and potentially harmful by increasing the risk of sepsis and aggravating postoperative dehydration.\textsuperscript{31} A 2-hour fasting period

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**Table 1: Comparison of duration of hospital stay in conventional surgery with fast-track surgery programmes**

<table>
<thead>
<tr>
<th>Operation</th>
<th>Conventional</th>
<th>Fast-track</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic cholecystectomy</td>
<td>3 days\textsuperscript{21}</td>
<td>1 day\textsuperscript{41}</td>
</tr>
<tr>
<td>Laparoscopic fundoplication for gastro-oesophageal reflux</td>
<td>2 days\textsuperscript{21}</td>
<td>1 day\textsuperscript{41}</td>
</tr>
<tr>
<td>Partial colectomy\textsuperscript{22}</td>
<td>6 - 12 days</td>
<td>2 days</td>
</tr>
<tr>
<td>Elective colorectal resection\textsuperscript{23}</td>
<td>8 - 12 days</td>
<td>2 - 5 days</td>
</tr>
<tr>
<td>Partial nephrectomy</td>
<td>3 - 10 days\textsuperscript{24}</td>
<td>2 - 6 days\textsuperscript{10}</td>
</tr>
<tr>
<td>Ileal pouch-rectal anastomosis\textsuperscript{11}</td>
<td>5 days</td>
<td>4 days</td>
</tr>
<tr>
<td>Cardiac surgery\textsuperscript{25}</td>
<td>9 - 14 days</td>
<td>8 - 12 days</td>
</tr>
<tr>
<td>Open aortic surgery\textsuperscript{12,13,16}</td>
<td>9 days</td>
<td>5 days</td>
</tr>
<tr>
<td>Elective aortic aneurysm repair\textsuperscript{14}</td>
<td>6 - 10 days</td>
<td>3 - 4 days</td>
</tr>
<tr>
<td>Carotid endarterectomy\textsuperscript{17}</td>
<td>4 days</td>
<td>1 - 2 days</td>
</tr>
<tr>
<td>Laparoscopic/vaginal hysterectomy</td>
<td>1 - 3 days\textsuperscript{20}</td>
<td>1 day\textsuperscript{11}</td>
</tr>
</tbody>
</table>

**Table 2: Patient care strategies**

**Preoperative**

- Patient selection and assessment
- Patient education
- No bowel preparation
- No fasting
- Preoperative fluid and carbohydrate loading
- Nutritional support

**Intraoperative**

- Surgical stress reduction
- Prophylactic antibiotics
- Perioperative oxygen therapy
- Optimising anaesthesia
- Minimally invasive techniques
- Normothermia
- Limited use of tubes, drains and catheters

**Postoperative**

- Effective pain control
- Non-opiate oral analgesics — control of ileus
- Prophylaxis for nausea and vomiting
- Early mobilisation and nursing care
- Early oral feeding and dietary supplementation
- Early catheter removal
- Discharge planning
is recommended at present for elective surgery in patients without further risk for aspiration, until which oral rehydration therapy via clear fluids is safe and feasible.\[32\] In addition, 150 ml of clear carbohydrate fluids 2 hours prior to elective surgical procedures has shown to increase patient comfort by alleviating thirst, hunger and anxiety through the release of endogenous opioids, which also reduces the amount of intraoperative anaesthesia needed.\[33\] This also has beneficial effects in countering the insulin resistance arising as a result of surgical stress,\[34\] slightly reducing perioperative muscle catabolism\[1\] and promoting gastric emptying.\[35\] In cases of a malnourished patient, particularly those undergoing a major surgery, the preoperative nutritional support would be highly beneficial.

Pre-medication in a fast-track setting aims at reducing physiological stress responses to surgery. Alpha2-agonists and beta-blockers have been proven beneficial for the same. Alpha2-agonists such as clonidine and dexmedetomidine have been shown to have opioid-sparing effects when used as pre-medication. They also reduce intraoperative blood loss, perioperative myocardial ischaemia, shorten the duration of ileus\[36\] and improve pain control and PONV. Beta-blockers suppress the release of catecholamines, thereby reducing cardiovascular morbidity associated with surgery. They also have analgesic-sparing and anti-catabolic properties, which contribute to accelerated postoperative recovery.\[1\]

**Intraoperative strategies**

Optimisation of anaesthesia aims at achieving rapid postoperative recovery with minimal opioid effects postoperatively. Overly deep anaesthesia exacerbates the surgery-induced stress response and postoperative organ dysfunction thus attaining the optimal depth of anaesthesia is important in reducing morbidity and the time to total recovery.\[34\] Short-acting anaesthetics and analgesics are therefore preferred. A vast amount of research has shown that regional aesthetic techniques that use local anaesthetics can reduce the classic pituitary, adrenocortical and sympathetic responses to surgery.\[2\] Neurogenic blockades techniques (either by administering a local anaesthetic in the spinal or epidural space or by using local anaesthetic techniques that block the nerve impulses from a specific area) improve postoperative nitrogen economy\[37\] and glucose intolerance but does not modify inflammatory or immunological responses. Epidural analgesia has been shown to be superior to intravenous narcotics in controlling postoperative pain in both open and laparoscopic colon surgery,\[7,38\] in addition reducing postoperative ileus,\[39,40\] preserving exercise capacity following laparotomy, accelerating ambulation and thereby reducing postoperative pulmonary complications. Perioperative systemic lidocaine is a convenient and inexpensive option for patients not suitable for epidural anaesthesia.\[41\] Total intravenous anaesthesia is favourable in reducing PONV.

The use of minimally invasive abdominal surgical techniques, such as laparoscopic cholecystectomy, have not reduced the early endocrine mediated metabolic response to surgery, but this approach has been associated with a slight decrease in various inflammatory responses and immunodysfunction, improved pulmonary function and reduced postoperative ileus.\[42,43\] However, the application of a combination of fast-track rehabilitation techniques may influence the outcome more than the choice between a laparoscopic technique versus ‘open’ operation per se.\[44\] The current evidence suggests that within a fast-track surgery programme, there is no difference between laparoscopic and open surgery in terms of postoperative recovery rates or length of hospital stay. However, minimally invasive surgery does reduce inflammatory responses, pain and catabolism due to the reduced wound size.\[42,45\] In open abdominal surgery, pain and pulmonary dysfunction have been proved to be reduced in cases where transverse and oblique incisions are used instead of a long vertical incision, which may be due to fewer dermatomes affected.

Fluid management must be carefully optimised, as both over hydration and fluid restriction cause their own set of problems. While perioperative administration of liberal amounts of fluid has been shown to reduce nausea, vomiting, dizziness, drowsiness and thirst, excessive hydration may potentially lead to pulmonary and cardiac dysfunction. Excessive hydration also impairs wound healing, particularly in case of anastomoses, by reducing tissue oxygenation. In contrast, restricted fluid intake can cause inadequate organ perfusion via reduction of the effective circulating volume. Therefore, fluid management has to be customised for every patient and goal-directed as the individual preoperative hydration statuses and surgical stress responses vary. Objective assessment of the individual fluid requirement can be done by successive challenges of a small amount of colloid preoperatively and postoperatively and measurement of corresponding changes in stroke volume (and therefore the cardiac output), which can be measured using oesophageal Doppler or pulse pressure.\[46,47\] Improvement in postoperative outcome using this approach has been demonstrated by several randomised trials.\[48,49\] Intraoperative volume therapy is based on administration of colloids and avoidance of excessive crystalloids. Using a combination of crystalloids and colloids avoids intraoperative hypovolaemia while avoiding excessive crystalloids. Similar to overnight fasting, overnight fluid restriction
can be avoided to prevent the preoperative hypovolaemia and requirement for intraoperative volume replacement. As per the enhanced recovery after surgery protocol, oral fluid intake of more than 300 ml of fluid on the day of surgery is recommended along with cessation of intravenous fluids on postoperative day 1.\textsuperscript{[50]}

**INTRAOPERATIVE NORMOTHERMIA**

Patients undergoing surgery often become hypothermic due to cold operating rooms, inadequate clothing cover and anaesthetics, which hamper their homeostatic defences to cold. As a result, patients undergoing operations lasting over 2 hours often suffer a fall of core temperature of 2 - 4°C, particularly in thoracic and abdominal surgeries. Perioperative hypothermia triples the incidence of adverse myocardial outcomes, increases blood loss due to impaired haemostasis, delayed metabolism of anaesthetic drugs with delayed recovery and the increased incidence of surgical wound infection. In addition, during re-warming, cortisol and catecholamines are released, which augment the stress response of the operation. Keeping patients warm has been associated with a 3-fold decrease in the rate of wound infection, a reduction in operative blood loss, a decrease in untoward cardiac events and a reduction in nitrogen excretion and patient discomfort. Maintenance of intraoperative normothermia is achieved by active warming of the patient using intraoperative hot air warming blankets, which cover the non-operated parts of the body, administration of warm intravenous fluids, forced-air and resistive heating.\textsuperscript{[51]}

Nausea and vomiting are frequent after administration of general anaesthesia and abdominal surgery. PONV delay recovery by prolonging the time taken to resume oral hydration and feeding. Prevention of PONV begins intraoperatively by avoiding drugs that cause PONV and volatile anaesthetic agents or administering them in reduced doses. The use of a multi-modal approach using prophylactic antiemetics with adequate hydration is associated with improved patient compliance.\textsuperscript{[52]}

Perioperative oxygen therapy appears to be a potentially effective intervention that may provide a significant reduction in the occurrence of surgical site infection, particularly in patients undergoing colorectal surgery. However, its utility and scope require further study as potential deleterious effects of high FIO\textsubscript{2} oxygen therapy have also been described.\textsuperscript{[53-56]}

**POSTOPERATIVE STRATEGIES**

**Pain control**

Postoperative pain amplifies the surgical stress response and organ dysfunction and delays recovery.\textsuperscript{[57]} It hinders postoperative mobilisation and the resumption of daily activities. Major surgical procedures with high intensity pain therefore require the use of invasive analgesic methods, such as continuous epidural analgesia, to hasten recovery.\textsuperscript{[58]} Based on a systematic review of postoperative analgesia, the effect of choice of postoperative analgesia on postoperative mortality or morbidity has not been established. However, the use of epidural analgesia along with local anaesthetics has been repeatedly associated with faster resolution of postoperative ileus after major abdominal surgery. The site of an epidural must be appropriate to the level of surgical incision. It is advisable to remove epidural catheters before 3 days elapse following their placement and to avoid repositioning or removal and replacement as there is a substantial risk of infection.\textsuperscript{[59]} Supplemental non-steroidal anti-inflammatory drugs can be used to treat pain not covered by the epidural.

Multi-modal analgesia combines multiple agents, opioid with non-opioids, like ketorolac and provides successful pain control with good patient satisfaction and decreased postoperative urinary retention.\textsuperscript{[60-62]} The principle of multi-modal or balanced analgesia is to gain additive effects from different modalities of pain control while minimising the side effects, particularly those of opioids (such as sedation, nausea, ileus and urinary retention), which hamper both early mobilisation and enteral nutrition. Several agents such as non-steroidal anti-inflammatory drugs, COX-2 inhibitors, ketamine, gabapentin and local anaesthetics have been evaluated for their utility in reducing the use of opioids for analgesia.\textsuperscript{[27]} Optimal management of acute pain following major procedures is a prerequisite for fast-track surgery as it facilitates early discharge. Hospital-level pain management protocols should be established along with regular evaluation of pain and its documentation.

**Early enteral nutrition**

The importance of patient nutrition has been emphasised in the preoperative period. Adequate postoperative nutrition is equally important as it enhances wound healing, reduces fatigue and muscle wasting and the risk of infection. Oral intake is traditionally limited in the postoperative period and involves a gradual transition from liquid to solid feeds. Especially in cases of bowel anastomosis, caution is usually exercised while proceeding with oral feeds. However, several studies have shown that early oral intake is safe even after bowel resection,\textsuperscript{[63]} as early enteral nutrition reduces gut permeability, which also reduces infection by reducing bacterial translocation.\textsuperscript{[1,64]} Limiting oral intake in the postoperative period is not necessary even after colonic procedures using an anastomosis if epidural anaesthesia is used as it attenuates ileus.
Postoperative ileus, which is predominantly caused by a combination of inhibitory neural sympathetic visceral reflexes and the intestinal inflammatory response, increases pain and discomfort and delays early mobilisation and oral intake. It may be considerably alleviated by a combination of epidural local anaesthetics, opioid-sparing analgesia, minimally invasive surgery, minimising bowel handling, avoidance of routine nasogastric tubes, early feeding and pharmacotherapy.\(^{[62,65]}\) The greatest reduction in perioperative pain management, combinations of analgesia, early enteral nutrition and early mobilisation that counteract fatigue associated with surgery and reduce the incidence of postoperative complications. There is, however, a need for continued study of the basic mechanisms of the surgical stress responses in order to develop interventions that counteract specifically their unfavourable aspects while preserving the aspects required for recovery, such as wound healing and immune responses. Innovations in minimally invasive surgery, pharmacological modulation of surgery-related inflammation and anaesthetic techniques are necessary to further improve the fast-track programmes.

**Tubes and drains**

Several trials and meta-analyses\(^{[60,66]}\) have confirmed the lack of added benefit in utilising nasogastric tubes as a routine. They should be particularly avoided in a fast-track programme as they have been found to increase the incidence of pneumonia in addition to extending the duration of hospital stay. Patients managed without nasogastric tubes need fewer days to resume oral intake.\(^{[67]}\) Oral intake can often be successfully initiated 6 hours following surgery.\(^{[7]}\) Studies have also advocated against the routine use of surgical site drains as they may slow the return of bowel function and hinder effective pain control.\(^{[1,64-71]}\)

In case of patients undergoing anorectal surgery, urinary retention is a common complication postoperatively. The risk factors contributing to urinary retention include excessive intravenous fluid administration and inadequate pain relief.\(^{[72]}\) Therefore, besides good analgesia, intraoperative intravenous fluid restriction must be considered to prevent urinary retention.

Early mobilisation is a universal component of any fast-track plan. Prolonged bed rest increases muscle wasting, predisposes to pulmonary dysfunction, infections and thromboembolism.\(^{[68]}\) Significant improvement on follow-up was found in parameters such as fatigue, sleep, return to leisure activity and activities of daily living following early mobilisation.\(^{[73]}\) Postoperative ambulation and movement should be fully encouraged and facilitated by means of adequate pain relief.

**CONCLUSION**

Results from studies of fast-track programmes employing a multi-modal approach have shown improved outcomes, particularly fast-track colorectal programmes.\(^{[24-76]}\) The reduction of surgical stress and the length of hospital stay are the primary objectives of these programmes. This is achieved by the implementation of improved perioperative pain management, combinations of anaesthesia and analgesia, early enteral nutrition and early mobilisation that counteract fatigue associated with surgery and reduce the incidence of postoperative complications. There is, however, a need for continued study of the basic mechanisms of the surgical stress responses in order to develop interventions that counteract specifically their unfavourable aspects while preserving the aspects required for recovery, such as wound healing and immune responses. Innovations in minimally invasive surgery, pharmacological modulation of surgery-related inflammation and anaesthetic techniques are necessary to further improve the fast-track programmes.
defined parameters. The provision of information and education on the principles of the fast-track concept must be intensified along with refinement of its individual components. This would pave way for a more widespread understanding and materialisation of these strategies.

REFERENCES


54. Dellinger EP. Increasing inspired oxygen to decrease surgical site infection: Time to shift the quality improvement research paradigm. JAMA 2005;294:2091-2.


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Assessment and modifications of digestion procedures to determine trace elements in urine of hypertensive and diabetes mellitus patients

Awad Abdalla Momen¹,², Mohammed Awad Ali Khalid¹,³, Malik Abdalla Abdelrahman Elsheikh¹,⁴, Dafaalla Mohamed Hag Ali¹,⁴

¹Department of Chemistry, Faculty of Applied Medical Sciences – Turabah Branch, Taif University, Taif, Saudi Arabia, ²Department of Chemistry, College of Applied and Industrial Sciences, Bahri University, ³Department of Chemistry, Faculty of Science, University of Khartoum, ⁴Department of Chemistry, College of Science, Sudan University of Science and Technology, Khartoum, Sudan

ABSTRACT

Context: There is accumulating evidence that the metabolism of several trace elements like Cr, Cu, Pb, Cd, Co, Mn and Zn might have specific roles in the pathogenesis and progress of many diseases like hypertension (HTN) and diabetes mellitus (DM).

Objectives: To provide a fast, efficient, sensitive, and reliable analytical procedure for trace element determination in urine samples of HTN and DM patients using inductively coupled plasma optical emission spectrometry (ICP-OES).

Setting and Design: The ICP-OES operating conditions were optimised and carefully selected in order to maximise the sensitivity, precision and accuracy. Factors affecting analytical and biological variability of the concentrations under study were discussed and carefully optimised.

Materials and Methods: Different digestion procedures with acids and oxidising reagents were tested. The suitable procedure ICP-OES was selected, carefully modified and applied. The validity and accuracy of the different elements were determined by spiking of samples with known amounts of multi-element standard solution.

Statistical Analysis: Student t-test and analysis of variance (ANOVA) test were used for analysis. Microsoft Excel was used to assess the significance of the difference between variables. The concentrations obtained were expressed as mean value ± standard deviation (P = 0.05).

Results: The results of this study showed that the mean concentrations of Cd, Zn, Pb, Cu, Cr and Mn in urine from both HTN (study group A) and DM (study group B) patients were higher than the corresponding values observed in the control group. However, while the mean value of Co was low as compared to the control group, the differences found were not significant (P = 0.05).

Conclusion: The method used had excellent sensitivity, multi-element data could be obtained with very short acquisition time. The elements Cr, Cd, Pb and Zn might have specific roles in the pathogenesis and progress of HTN and DM. Further studies are required to investigate the possible roles of these elements in HTN and DM individuals.

Keywords: Diabetes mellitus, digestion procedures, hypertension, urine, trace elements

INTRODUCTION

Hypertension (HTN) is the force exerted by blood against the walls of the blood vessels. It is characterised by the increase of pressure in blood vessels. The prevalence of HTN increases with advancing age. However, nowadays the age criteria have been changed and even the young have HTN problems due to lack of exercise, fast foods, coffee consumption, smoking, alcohol use, etc. Genetic effects may also be a factor.¹,² On the other hand, diabetes mellitus (DM) is a disease that occurs all over the world, however, its prevalence rates differ from one country to another. It is characterised by a disorder of glucose metabolism associated with a reduced ability...
of tissues to respond to insulin. The hormone insulin, produced by the pancreas, helps the glucose to enter the cells where it is used as fuel by the body. In DM patients, the body’s metabolic process is completely disturbed either due to lack of insulin or due to ineffectiveness of the insulin produced by the body. Moreover, clinical research suggests that the homeostasis of trace elements can be disrupted by different diseases such as HTN and DM. According to their abundance, these elements are classified as macro-, micro- or trace elements. The remaining could be attributed to those elements with unknown biological functions, to others which are present only because of the exposure to polluted environment or to those intentionally introduced into the body for special purposes.

Current development of human health related studies requires a growing number of elements to be monitored in biological samples. Few of the elements present in nature play a metabolic role in living organisms. According to their abundance, these elements are classified as macro-, micro- or trace elements. The remaining could be attributed to those elements with unknown biological functions, to others which are present only because of the exposure to polluted environment or to those intentionally introduced into the body for special purposes.

Trace elements have recently been attracting the attention of scientists in various systems related to human health such as clinical and environmental analysis. Additionally, the measurement of trace elements is increasingly attracting the interest of physicians because deviations in trace element uptake and/or metabolism are known to be related to certain diseases. Analytical studies of trace elements dealing with problems of microanalysis of biological samples also have been increasing due to the expanding health areas. However, great efforts have been made developing analytical procedures for trace element measurement and improving their sensitivity and specificity.

The abnormal metabolism of trace elements plays an important role in health and disease conditions, and studies about them have been attracting significant interest. It has been speculated that trace elements may play a role in the pathogenesis of many diseases. Some of them form part of enzymes and others are involved in the synthesis of hormones. Others are known to be associated with certain diseases if they are present in the body in abnormally low concentrations. Several have been documented as being involved in blood pressure control while some may lead to intoxications in humans if ingested in high concentrations. Many of them are excreted primarily in urine and some are transmitted to blood.

Urine usually is used for the diagnosis of chronic degenerative disease that is caused by some trace elements. Therefore, urine analysis can provide important information to a clinician that may not be readily available with blood analysis. The levels of trace elements in the blood and urine are tightly controlled via metabolic, reabsorptive and excretory mechanisms.

Bone and teeth, hair and nails, organs and blood and its components (urine, cerebrospinal, amniotic, synovial fluids and tears, saliva, perspiration, bile, milk) are good indices of exposure to elements and can easily be assessed thus making them suitable to be used as bioindicators for these purposes. According to the above facts, it is important to determine the trace element concentrations in human urine having physiological disorders, like HTN and DM. Therefore, human urine was chosen for this study as probability (representative) sampling. Sample collections consisted of a number of healthy (control group) and HTN and DM individuals (study groups A and B) of different ages (30 - 75 yrs), which were selected from occupants of urban populations from Taif, Saudi Arabia on personal request. A questionnaire was employed to collect details concerning physical data, ethnic origin, health, dietary habits and consent of donor. Some factors affecting analytical and biological variability of the concentrations to be determined, such as the route of absorption, the presence of sources of environmental pollution in certain areas of residence, physiological variables and lifestyles, were also discussed.

There are several modern techniques for the determination of trace elements in urine. The digestion procedures vary according to the nature of the samples, the available method of analysis, elements to be determined and their concentration levels. Most techniques generally require the element to be in soluble forms. In all cases, samples demand manipulation prior to other processing and detection. In most inorganic determinations in clinical researches, the sample is digested or leached by oxidising acidic mixtures aided by heat or ultrasound or microwave radiation for oxidising the organic matter. The main advantages of microwave-assisted procedures were that it required smaller amounts of sample and oxidising materials, shorter digestion times, and easiness of sample handling. These procedures had to be validated to ensure that no contamination and/or losses occurred. The presence of these problems could affect the accuracy and provision of the final results. Therefore, the validation of the whole procedure was made by using a certified reference materials and/or standard additional method and/or by comparing the results of different certified analytical procedures.

Biomonitoring of such trace elements present in complex samples required sensitive analytical methods with outstanding precision and high sample throughput. This was to cope with the low element
concentrations and the large number of samples that were to be processed, eventually following an emergency.[10] The most common analytical technique for measuring trace elements concentrations in biological samples like urine are flame or electrothermal atomic absorption spectroscopy,[6,8,10,21-23] inductively coupled plasma optical emission spectroscopy (ICP-OES),[20,24] inductively coupled plasma mass spectrometry[14,25-30] and high performance liquid chromatography.[31]

It follows that analytical methods for determining minor and trace elements in biological matrices such as urine and blood should involve minimal sample handling and achieve relatively low detection limits, to permit easy and reliable determination of elements.[15] Considering these requirements, ICP-OES was a good solution, because it allowed rapid and precise multi-element determination in a single solution, with sufficiently low detection limits and wide dynamic range and high accuracy.[20,23,29,30]

Although potentially harmful effects of trace elements are generally well-known, limited studies are available regarding the investigation of the relationship between these elements and diseases. This will be indicated by determining the concentrations of selected trace elements like Cd and Pb in urine of HTN and DM individuals (study groups A and B). These concentrations will then be evaluated to determine the increase or decrease of these elements as compared to the control group. A total of 150 samples of urine were analysed after ‘wet digestion’ for seven trace elements using ICP-OES.

**MATERIALS AND METHODS**

**Instrumentation and conditions**

A Varian 725-ES, ICP-OES with radial viewing configuration was used to analyse the standard and sample solutions of Cd, Co, Cr, Cu, Mn, Pb and Zn. The ICP-OES operating conditions were well optimised and carefully selected in order to maximise the sensitivity for the desired elements and to obtain the best precision and accuracy. Details of the operating conditions are summarised in Table 1. Each element was measured at two specific lines (nm) atomic (I) and/or ionic (II) line characteristics of a particular element that gives maximum sensitivity.[24] Lead was measured only at atomic (I) line. The intensity of this emission is indicative of the concentration of the element within the samples. Selected emission lines (nm) for each element are summarised in Table 2.

**Reagents and glassware**

All reagents and chemicals were of analytical grade from Darmstadt, Germany. Mineral acids, chemical reagents, and oxidising agents [95 - 98% (m/m) H$_2$SO$_4$ (d = 1.84 - 1.85 kg l$^{-1}$), 69 - 72% (m/m) HNO$_3$ (d = 1.41 - 1.51 kg l$^{-1}$), 36.5 - 38% (m/m) HCl (d = 1.18 - 1.19 kg l$^{-1}$), 30% (m/m) H$_2$O$_2$ (d = 1.11 - 1.45 kg l$^{-1}$)], etc. were used. A multi-element stock standard solution (1,000 mg l$^{-1}$) was also used. Calibration standard solutions were obtained from the stock solution by suitable dilutions. Deionised doubly distilled water (DDDW), was also used throughout the analyses for preparing reagent, standard and sample solutions. DDDW was also used for washing and rinsing of all apparatus and glassware. Acid-washed plastic (polypropylene) vessels were used for preparing and storing solutions. All solutions were stored at −5°C until needed for analysis. Plastic, glassware and the auto sampler cups were cleaned by soaking in 5 mole l$^{-1}$ HNO$_3$ for about 24 hrs, rinsing five times with DDDW, dried, and stored in a class (100 laminar) flow hood.

**Collection of samples**

For the present study, samples of human urine were collected from healthy non-smoking control (n = 50), HTN (study group A; n = 50) and DM (study group B; n = 50) individuals in a polyethylene storage bottles (acid cleaned bottles). Samples were taken from males and females of different ages ranged from 30 - 75 yrs from occupants of urban populations from Taif, Saudi

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**Table 1: ICP-OES operating parameters for determination of trace elements in urine samples**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF Power (KW)</td>
<td>1.2</td>
</tr>
<tr>
<td>Nebuliser pressure (KPa)</td>
<td>250.0</td>
</tr>
<tr>
<td>Viewing high (mm)</td>
<td>10.0</td>
</tr>
<tr>
<td>Plasma gas flow rate (l min$^{-1}$)</td>
<td>15.0</td>
</tr>
<tr>
<td>Auxiliary gas flow rate (l min$^{-1}$)</td>
<td>1.5</td>
</tr>
<tr>
<td>Sample uptake rate (ml min$^{-1}$)</td>
<td>0.8</td>
</tr>
<tr>
<td>Sample uptake delay (sec)</td>
<td>30</td>
</tr>
<tr>
<td>Instrument stabilisation delay (sec)</td>
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</tr>
<tr>
<td>Pump rate (rpm)</td>
<td>20</td>
</tr>
<tr>
<td>Rinse time (sec)</td>
<td>20</td>
</tr>
<tr>
<td>Replicates (times)</td>
<td>3</td>
</tr>
<tr>
<td>Replicate read time (sec)</td>
<td>7</td>
</tr>
</tbody>
</table>

**Table 2: ICP-OES selected atomic (I) and/or ionic (II) emission lines (nm) for each element**

<table>
<thead>
<tr>
<th>Atomic (I) lines</th>
<th>Ionic (II) lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cd 214.439</td>
<td>Cd 226.502</td>
</tr>
<tr>
<td>Co 237.863</td>
<td>Co 238.892</td>
</tr>
<tr>
<td>Cr 267.716</td>
<td>Cr 284.325</td>
</tr>
<tr>
<td>Cu 324.754</td>
<td>Cu 327.395</td>
</tr>
<tr>
<td>Mn 257.610</td>
<td>Mn 293.305</td>
</tr>
<tr>
<td>Zn 202.548</td>
<td>Zn 213.857</td>
</tr>
<tr>
<td>Pb 220.353</td>
<td>—</td>
</tr>
</tbody>
</table>
Arabia. Samples were kept in the freezer (−5°C) till further analysis.

**Microwave acid digestion**

Triplicate of 0.5 ml of human urine samples, of each HTN (study group A), DM (study group B) and control group were directly placed into a porcelain crucible. Three millilitres of a freshly prepared mixture concentrated HNO$_3$ – H$_2$O$_2$ (2:1, v/v) was added to each crucible. The crucibles were covered and kept at room temperature (~35°C) for about 5 mins as a predigestion time, then placed in a microwave oven. Then, crucibles were heated following a one-stage digestion program at 30% of total power (900 W). Complete digestions of all samples required 2 - 3 mins. After the digestion was completed, the crucibles were left to cool at room temperature and the resulting solution (about 0.5 ml of semi-dried mass) was dissolved by 5 ml of 0.1 mole l$^{-1}$ HNO$_3$. This was then, transferred quantitatively to 10 ml volumetric flasks, diluted with DDDW up to mark and transferred to a polyethylene storage bottle for further analysis. Blank and spike sample solutions were carried out simultaneously through the complete digestion procedures and similar acid matrices. The presence of Ca. 0.1 mole l$^{-1}$ HNO$_3$ in the final solution was necessary to maintain acidic environment and avoid formation of insoluble hydroxides before measurement steps. This procedure is similar to that stated by Kazi,[14] Afridi[13] and Memon,[21] with some modifications in digestion time and microwave oven program. The validity of the digestion procedure was checked by spiking of different samples with known amounts of multi-element standard solution before and after digestion procedures. All selected trace elements were determined in the prepared solutions by ICP-OES.

**Statistical analysis**

All results were statistically evaluated by Student $t$-test, and ANOVA test ($P = 0.05$). In addition, Microsoft Excel and Origin software’s were also used to assess the significance of the differences between the variables investigated in patients and control individuals. The concentration values obtained were expressed as average value ± confidence interval ($P = 0.05$). All statistical analysis was based upon triplicate measurements of all standard and sample solutions.

**Analytical figures of merit**

The validity and efficiency of the microwave digestion method was checked by analysing spike solutions with a multi-element standard solution. The spike solutions were added to known amounts of the samples before and after digestion, which had also been through the digestion steps. The detection limit (LOD) was defined as 3 s m$^{-1}$, where SD is the standard deviation corresponding to 10 blank injections and m is the slope of the calibration graph. The LOD was 5 μg l$^{-1}$ for Pb, 1 μg l$^{-1}$ for Cu and Co, 0.9 μg l$^{-1}$ for Cr, 0.6 μg l$^{-1}$ for Cd, 0.5 μg l$^{-1}$ for Zn and 0.08 μg l$^{-1}$ for Mn.

**RESULTS AND DISCUSSION**

All results were expressed as x ± SD, where x is the mean values and SD is the standard deviation. To ensure that no contamination and/or loss of elements occurred during sample preparations and measurement methodology, a recovery test was demonstrated by standard addition methodology. It was performed using a bulk sample which had also been through all the digestion procedures. Multi-element standard solution spike were added to a known amount of the samples both before and after digestion, to assess the validity of the digestion procedure. The recoveries of the predigested spiked sample ranged between 95.8 - 103.7%; while, the recoveries of the postdigested spiked samples were between 95.7 - 102.8%. This indicated that there was no occurrence of contamination and/or loss of elements during sample preparations and measurement steps. Therefore, no significant differences were observed in measured values ($P = 0.05$).

Table 3 shows the results that were obtained for the determined trace elements in urine samples of the control group, HTN (study group A) and DM (study group B). According to the results, it was found that the levels of Zn (1.64 ± 0.25 mg l$^{-1}$) and Cu (0.48 ± 0.08 mg l$^{-1}$) in urine of HTN (study group A) were high as compared with to the corresponding values of control group (0.95 ± 0.14 mg l$^{-1}$) and (0.18 ± 0.04 mg l$^{-1}$), respectively. Likewise, the levels of Zn (1.78 ± 0.28 mg l$^{-1}$) and Cu (0.67 ± 0.11 mg l$^{-1}$) in urine of DM (study group B) were high as compared with the corresponding values of control group (0.95 ± 0.14 mg l$^{-1}$) and (0.18 ±

<table>
<thead>
<tr>
<th>Samples (urine)</th>
<th>Cd</th>
<th>Co</th>
<th>Cr</th>
<th>Cu</th>
<th>Mn</th>
<th>Pb</th>
<th>Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>0.12 ± 0.03*</td>
<td>1.22 ± 0.24</td>
<td>0.05 ± 0.02</td>
<td>0.18 ± 0.04</td>
<td>0.04 ± 0.02</td>
<td>0.34 ± 0.07</td>
<td>0.95 ± 0.14</td>
</tr>
<tr>
<td>HTN (study group A)</td>
<td>1.92 ± 0.29</td>
<td>0.45 ± 0.06</td>
<td>0.13 ± 0.03</td>
<td>0.48 ± 0.08</td>
<td>0.09 ± 0.03</td>
<td>1.01 ± 0.21</td>
<td>1.64 ± 0.25</td>
</tr>
<tr>
<td>DM (study group B)</td>
<td>1.02 ± 0.17</td>
<td>0.98 ± 0.18</td>
<td>0.11 ± 0.03</td>
<td>0.67 ± 0.11</td>
<td>0.07 ± 0.02</td>
<td>1.45 ± 0.26</td>
<td>1.78 ± 0.28</td>
</tr>
</tbody>
</table>

* A mean ± standard deviation (n = 3)
0.04 mg l$^{-1}$), respectively, but the differences found were not significant ($P = 0.05$).

Furthermore, it was found that the Cr levels in urine of HTN (study group A; 0.13 ± 0.03 mg l$^{-1}$) and DM (study group B; 0.11 ± 0.03 mg l$^{-1}$) were high as compared to the control group (0.05 ± 0.02 mg l$^{-1}$) with no significant differences ($P = 0.05$). Moreover, very close Mn values were detected in urine of HTN (study group A; 0.09 ± 0.03 mg l$^{-1}$) and DM (study group B; 0.07 ± 0.02 mg l$^{-1}$) as compared to the control group (0.04 ± 0.02 mg l$^{-1}$) but the differences found were non-significant ($P = 0.05$).

In contrast, low Co values were detected in urine of HTN (study group A; 0.45 ± 0.06 mg l$^{-1}$) and DM (study group B; 0.98 ± 0.18 mg l$^{-1}$), as compared to control group (1.22 ± 0.24 mg l$^{-1}$), but the differences found were insignificant ($P = 0.05$).

On the other hand, high levels of both Cd and Pb were detected in the urine of HTN (study group A; 1.92 ± 0.29 mg l$^{-1}$) and (study group A; 1.01 ± 0.21 mg l$^{-1}$) and DM (study group B; 1.02 ± 0.17 mg l$^{-1}$) and (study group B; 1.45 ± 0.26 mg l$^{-1}$), as compared to control group (0.12 ± 0.03 mg l$^{-1}$) and (0.34 ± 0.07 mg l$^{-1}$) respectively, but the differences found were not significant ($P = 0.05$).

Figure 1 shows the distribution of concentrations of seven selected trace elements in the urine of control, HTN and DM groups under study. It showed that lower concentrations were observed for Mn, Cr, Cu and Co. The opposite was true for Cd, Zn and Pb. Elevated value of Cd was observed in the urine of HTN individuals.

There are wide variations in the published data for the trace elements concentrations in biological samples such as urine of HTN and DM individuals of different countries.$^{[1,2,4,6,23,33-40]}$ To compare the reference ranges determined in the present study with those found by other authors is difficult, because there is a lack of coherence in the levels of trace elements found by various laboratories. One possible explanation for the different ranges of trace elements may come from the fact that with higher analytical sensitivity, the presence of contaminants becomes increasingly important. This is especially the case with elements that are physiologically present at very low concentrations, such as Mn, Cd, Pb and Zn.

**CONCLUSION**

The main goal of the work described here is to provide a fast, sensitive, and reliable method for trace elements analyses in a range of clinical matrices, i.e., urine (of HTN and DM individuals) using high resolution ICP-OES. To assess this, a suite of clinically important trace elements such as Cd, Co, Cr, Cu, Mn, Pb and Zn was quantified. However, after all conditions had been established, measurements became very efficient. Since the ICP-OES has excellent sensitivity, multi-element data can be obtained with very short acquisition time. Three replicates for seven trace elements were performed in only about 30 seconds, 150 samples of each of the seven trace elements were measured in a few hours (~2 hrs). We can conclude that there is accumulating evidence that the metabolism of several trace elements like Cr, Cu, Pb, Cd and Zn might have specific roles in the pathogenesis and progress of many diseases like HTN and DM.$^{[11]}$

**ACKNOWLEDGEMENT**

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**REFERENCES**


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Evaluation of selected trace elements in male type 2 diabetic patients in Nnewi, south eastern Nigeria

Christian Ejike Onah¹, Samuel Chukwuemeka Meludu²,³, Chudi Emmanuel Dioka³, Ubuo Kalu Amah³, John Ekenedirichukwu Okwara³, Charles Ukachukwu Osuji⁴

¹Department of Chemical Pathology, Nnamdi Azikiwe University Teaching Hospital, Nnewi, ²Department of Human Biochemistry, Faculty of Basic Medical Sciences, ³Department of Chemical Pathology, ⁴Department of Internal Medicine, Faculty of Medicine, Nnamdi Azikiwe University, Nnewi Campus, Nigeria

ABSTRACT

Background: There is accumulating evidence that the metabolism of several trace elements is altered in type 2 diabetic patients.
Aims: We, therefore, investigated the levels of some of the trace elements in serum of male type 2 diabetic patients with a view to establishing their metabolic status in these subjects.
Materials and Methods: One hundred and twenty-five male type 2 diabetic subjects and 50 apparently healthy non-diabetic male individuals within the age range of 32 - 70 years were recruited for this study. Fasting plasma glucose (FPG), trace elements (zinc, selenium, manganese and chromium), and body mass index (BMI) were determined.
Results: The mean levels of Zn, Mn, Se and Cr were significantly lower in serum of type 2 diabetic patients when compared with non-diabetic controls (P < 0.001). Expectedly, the mean level of FPG in diabetic subjects was significantly higher when compared with the healthy controls (P < 0.001) however, there was no significant different in the level of BMI (P > 0.05). This study also observed a significant negative correlation between the serum levels of Trace Elements (Zn, Se, Cr and Mn) and the FPG in diabetic subjects.
Conclusion: Consequently, the decrease in levels of trace elements may play a role in pathogenesis of diabetes mellitus considering their roles in glucose metabolism. Therefore, proper dietary control and mineral supplementation is advised.

Keywords: Metabolism, pathogenesis, supplementation, trace elements, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus is a metabolic disorders of carbohydrate metabolism in which glucose is underused, producing hyperglycaemia.[1] Diabetes affects over 150 million people worldwide and this number is expected to double by 2025,[2] 90% of whom are type 2.[3] As the disease progresses, patients are at increased risk for the development of specific complications, including retinopathy leading to blindness, nephropathy leading to renal failure, neuropathy (nerve damage), and atherosclerosis.[4]

The International Diabetes Federation (IDF) estimated in 2012 that 366 million adults, aged 20 - 79 years, out of the world’s 7 billion population have diabetes. This gives a comparative prevalence of 8.5%. In Africa, over 4.3% are estimated to have diabetes while 81.2% of Africans with diabetes are undiagnosed. This region has the highest mortality rate due to diabetes and it has been estimated that over the next 20 years, the number of people with diabetes in the region will almost double. According to the WHO standard, Nigeria has a comparative prevalence of 4.83% with over 88,681 diabetes-related deaths.[5] The work done by Osuji et al, on the prevalence of diabetes mellitus in a group of
Women attending “August meeting” at Naze South East Nigeria put the prevalence of diabetes at 6.7%.⁶

Trace elements are inorganic molecules which are essential for life. Although these elements constitute a relatively small amount of total body tissues, they are very essential in many physiological and biochemical processes. In states of absolute deficiency, death results and in limited intake biological functions are impaired.¹¹ Studies have shown that the metabolism of several essential trace elements is altered in diabetes and that these nutrients might have specific roles in the pathogenesis, complications and progress of this disease.⁷

Zinc (Zn) is an essential trace element that plays a vital role in maintaining many biological processes and cellular homeostasis. Zn plays a key role in the synthesis, secretion and action of insulin in both physiological and pathophysiological states.⁸ It also plays a critical structural role for antioxidant enzyme superoxide dismutase and can stabilize biological membranes to decrease their susceptibility to oxidative damage that can impair cell functions.⁹ Manganese(III) ions function as cofactors for a large variety of enzymes with many functions.¹⁰ Manganese (Mn) enzymes are particularly essential in detoxification of superoxide-free radicals in organisms that must deal with elemental oxygen. It also plays an essential part in sex hormone production, proper bone and cartilage formation, and glucose metabolism.¹¹

Chromium (Cr) is a well-known component of the glucose tolerance factor, which is involved in normal carbohydrate and lipid metabolism. It acts primarily by regulating insulin action; that is in the presence of Cr in physiological form, much lower amounts of insulin are required, since Cr acts by increasing insulin efficiency.¹² The selenium (Se) role in preventing glucose intolerance and the complications of diabetes mellitus has also been postulated. For instance, insulin reserves are decreased with Se deficiency causing glucose intolerance.¹³ Se is a potent antioxidant that acts as an anti-inflammatory agent and is required for immune system function.¹⁰ The biological functions associated with Se include male fertility, prevention of cancer, cardiovascular disease, viral mutation, endocrine and immune function as well as modulating inflammatory response.¹⁴

In view of all these putative roles, one can envisage that diminished levels of these trace elements may increase the severity of this disease. However, previous study has shown that appropriate trace element supplementation might prove beneficial in ameliorating some physiological deficiencies associated with diabetes and prevent or retard secondary complications.¹⁵

Since medications, genetics, medical conditions, lifestyle and dietary habits have been identified as the leading cause of type 2 diabetes mellitus and with the changing lifestyle and dietary trends in Nigeria, the prevalence of diabetes mellitus is bound to keep increasing with increasing effects on the metabolism of these trace elements. However, data concerning the level of trace elements in diabetic patient in South East Nigeria particularly in Anambra state is very scanty, hence the significance of this study. This study therefore, seeks to investigate the levels of some trace elements in male type 2 diabetic patient in our environment.

**MATERIALS AND METHODS**

**Study design and population**

This is a cross-sectional study designed to investigate the levels of trace elements in male type 2 diabetic patients and in non-diabetic controls. The study design received an approval from the Ethics Committee of Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi. The informed consents of all the participants were sorted and all the participants freely volunteered.

A total number of 175 participants were recruited for this study. The study population is 125 known type 2 diabetic male patients with mean age (51.58 ± 8.55) and age range (32 - 70 years) attending Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi (Eastern Nigeria) and 50 non-diabetic male individuals who are staff of the NAUTH, Nnewi with mean age (49.18 ± 11.46) and age range (32 - 70 years).

Among non-diabetic control group, those that are under mineral supplements, consume alcohol or smoke cigarette regularly or have any form of chronic illness such as hypertension, renal disease, heart problems, etc., were disqualified. Out of 53 control individuals that were finally selected three were disqualified based on their fasting plasma glucose that are above 7.0 mmol/L as recommended by WHO.¹⁶

All male patients with type 2 diabetes mellitus were considered eligible for this study, irrespective of age, duration of diabetes and treatment except those that take mineral supplements, drink alcohol or smoke cigarette regularly. The diagnosis of diabetes mellitus was made based on the World Health Organization criteria: two fasting glucose measurements above 7.0 mmol/L were considered diagnostic for diabetes mellitus.¹⁶ Patients’ medical history such as age, diabetes treatment and...
duration of diabetes were obtained. Their BMI were calculated using their measured height and weight.

The minimum sample size for the study was calculated using the formula when population is more than 10000.\[17\]

\[ n = \frac{Z^2pq}{d^2} \]

where \( n \) = minimum sample size; \( Z \) = standard normal deviation at 95% confidence interval is 1.96; \( p \) = proportion of the population estimated to have the public health problem under study (the prevalence of diabetes in Nigeria is 4.83%).\[5\]

\[ q = 1 - p = 1 - 0.0483 = 0.95 \]

\[ n = \frac{(1.96)^2 (0.0483)(0.95)}{(0.05)^2} = 70.5 \]

**Blood sample collection and biochemical analysis**

Five millilitres of fasting venous blood samples were collected from all respondents for the analysis. A part was dispensed into fluoride oxalate bottles for glucose determination using standard enzymatic spectrophotometric method (Glucose Oxidase method). The remaining part was dispensed into a plain bottle and allowed to clot, retract and the serum stored at –20ºC until analysis of trace elements using Atomic Absorption Spectrophotometric method.

**Reference values for Trace Elements**

Zn: up to 1000 mcg/l.\[18\]

Mn: 0.3 - 1.04 mcg/l.\[19\]

Se: 50 - 145 mcg/l.\[20\]

Cr: 0.05 - 0.48 mcg/l.\[19\]

**Statistical analysis**

The version 20 of Statistical Package for Social Sciences (SPSS) was used in statistical analysis. All data were expressed as the mean ± standard deviations. Association between two variables was determined using Pearson’s correlation coefficient. Student’s t-test was used when comparing two groups. Differences with \( P \)-values <0.05 were considered significant.

**RESULTS**

One hundred and twenty-five diabetic patients were studied. Out of this number 91 (72.8%) were in oral hypoglycaemics, 15 (12.0%) were in insulin therapy and 19 (15.2%) were in combined therapy. The mean age and BMI of diabetic subjects were 51.58 ± 8.55 years and 25.31 ± 2.72 kg/m² respectively while that of control subjects were 49.18 ± 11.46 years and 25.1 ± 1.6 kg/m² respectively. The mean duration of diabetes (DDM) was 7.68 ± 5.73 years and the range was 1 - 22 years.

The results showed that the mean values of Zn, Mn, Se, and Cr were significantly lower in serum of diabetic patients when compared with the non-diabetic controls. Expectedly, the mean FPG was significantly higher in diabetic subjects when compared with the healthy controls. However, the mean BMI of the type 2 diabetic subjects was not significantly different to that of the healthy controls [Table 1].

The BMI, age, and DDM did not show any significant correlation with the Trace Elements (Zn, Se, Mn and Cr) in both Type 2 diabetic subjects and non-diabetic controls except Zn that showed a moderately significant negative correlation with Age in Type 2 diabetic subjects [Table 2]. In the same way, the FPG did not show significant correlation with the Trace Elements in non diabetic control subjects [Table 2]; however, FPG showed significant negative correlation with Trace Elements in diabetic subjects [Figures 1 - 4].

<table>
<thead>
<tr>
<th>Table 1: Age, BMI, FPG, and Trace Elements (Zn, Mn, Se, and Cr) in Type 2 diabetic subjects and in non-diabetic controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
</tr>
<tr>
<td>FPG (mmol/l)</td>
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<tr>
<td>Zn (mcg/l)</td>
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<tr>
<td>Mn (mcg/l)</td>
</tr>
<tr>
<td>Se (mcg/l)</td>
</tr>
<tr>
<td>Ch (mcg/l)</td>
</tr>
</tbody>
</table>

**Figure 1: Association between FPG and Manganese in Type 2 diabetic subjects**
DISCUSSION

Interest in the clinical significance of trace element metabolism has been steadily increasing. Trace elements have important physiological effects when present at concentrations other than those associated with classical toxicity or with extreme deficiency.\(^{[21]}\) There is accumulating evidence that the metabolism of several trace elements is altered in diabetes mellitus.\(^{[7,22]}\)

In this study, there was a significantly lower Zn level in diabetic subjects than in normal controls. This agrees with the works done by other researchers.\(^{[23-26]}\) Zn homoeostasis is mostly affected by hyperglycaemia which results in hyperzincuria or decreased gastrointestinal absorption of Zn or even both. El-Yazigi et al., evaluated both type 1 and type 2 diabetes and found that Zn excretion were greater in diabetes than in matched controls.\(^{[27]}\) It has been postulated that hyperglycaemia interferes with the active transport of Zn back into the renal tubular cells. In dogs, experimentally-induced hyperglycaemia resulted in significant hyperzincuria.\(^{[28]}\) In streptozotocin-induced diabetic rats, increased Zn excretion has been routinely observed.\(^{[29]}\) Even when the hyperglycaemia was reduced by the administration of insulin, hyperzincuria had been reported to persist though on a reduced level.\(^{[30,31]}\)

However, some studies have suggested a defect in Zn absorption associated with hyperglycaemia or diabetes. Kinlaw et al., demonstrated abnormal Zn tolerance tests in diabetic patients suggestive of decreased absorption.\(^{[30]}\) Escobar et al also demonstrated a down regulation of fractional Zn transport which may be related to increased production of metallothionein in diabetics.\(^{[32]}\) In relation to insulin, Quarteman demonstrated that diet induced Zn deficiency in rats, resulted in a decreased ability of the pancreas to secrete insulin in response to a glucose load.\(^{[33]}\) Thereafter, Boquist et al., demonstrated a decrease in glucose tolerance with no change in insulin production in Zn-deficient hamsters in response to an intra-venous glucose load.\(^{[34]}\) These suggest that Zn deficiency may reduce the ability of the pancreas to secret insulin in response to a glucose load.

Cr increases glucose tolerance by enhancing insulin efficiency.\(^{[12]}\) This present study showed a significant decrease in mean levels of serum Cr in type 2 diabetic subjects than in normal controls. This agreed with the work done by Anderson et al., which showed Cr deficiency in type 2 diabetic subjects.\(^{[35]}\) The reduction in levels of Cr in type 2 diabetes might be due to high level of glucose since hyperglycaemia have been suggested to increase the excretion of Cr.\(^{[35]}\) Thus, it
may not be surprising to find an inverse relationship between serum Cr levels and FPG in type 2 diabetic subjects as noted in this study.

Table 2: Association between BMI, Age, DDM, FPG, and Trace elements in type 2 diabetic subjects and normal controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Type 2 Diabetic Subjects</th>
<th>Non-diabetic control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI (kg/m²)</td>
<td>Age (years)</td>
</tr>
<tr>
<td>Zn (mcg/l)</td>
<td>$r = -0.071$</td>
<td>$r = -0.251$</td>
</tr>
<tr>
<td></td>
<td>$P = 0.432$</td>
<td>$P = 0.01$</td>
</tr>
<tr>
<td>Se (mcg/l)</td>
<td>$r = -0.095$</td>
<td>$r = -0.059$</td>
</tr>
<tr>
<td></td>
<td>$P = 0.291$</td>
<td>$P = 0.516$</td>
</tr>
<tr>
<td>Cr (mcg/l)</td>
<td>$r = -0.044$</td>
<td>$r = -0.096$</td>
</tr>
<tr>
<td></td>
<td>$P = 0.630$</td>
<td>$P = 0.285$</td>
</tr>
<tr>
<td>Mn (mcg/l)</td>
<td>$r = 0.103$</td>
<td>$r = 0.003$</td>
</tr>
<tr>
<td></td>
<td>$P = 0.254$</td>
<td>$P = 0.976$</td>
</tr>
</tbody>
</table>

CONCLUSIONS

In this study we found that serum levels of Trace Elements (Zn, Se, Cr, and Mn) were significantly lower in type 2 diabetic patients than in non-diabetic controls while there was no significant difference in the levels of BMI in both type 2 diabetic subjects and controls. This study also observed significant negative correlations between the serum levels of Trace Elements (Zn, Se, Cr and Mn) and the FPG in diabetic subjects. These observations might be as a result of poor glycaemic control. However, these observed low levels of Trace Elements in diabetics may play a role in the pathogenesis of diabetes mellitus considering their roles in glucose metabolism. Therefore, proper dietary control and mineral supplementation are advised. We advocate further clinical study that will involve larger study population and HbA$_1c$ measurement with more sophisticated techniques in order to fully understand the role of Trace Elements in Type 2 diabetes mellitus.

REFERENCES

Incidental caseating granuloma of thyroid gland presenting with concomitant Graves’ disease and multifocal papillary microcarcinoma

Muneera A Al Shareef, Murthuza Patan Khan, Khalid S Al-Jabri, Ali A Eltayeb

Departments of Endocrinology, and Pathology, King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia

ABSTRACT
A 36-year-old Saudi woman presented with symptoms and signs of hyperthyroidism and was diagnosed to have Graves’ disease. She was initially treated with antithyroid medications with no response. Subsequently, she underwent a total thyroidectomy. The histopathology of the specimen revealed caseating granulomatous thyroid suggestive of tuberculosis and multifocal papillary thyroid microcarcinoma

Keywords: Caseating granulomatous thyroiditis, Graves disease, papillary carcinoma of thyroid

INTRODUCTION
Well-differentiated thyroid cancer and Graves’ disease have been reported in several cases; however, the presence of concomitant TB has not been described in the literature. We report a case with a combination of all three pathologies in thyroid tissue with a review of literature.

CASE REPORT
A 36-year-old woman presented with palpitations, heat intolerance, weight loss and insomnia. On clinical examination, she was anxious with a pulse rate of 110/min regular, and blood pressure 138/87 mmHg. She had tremors in her hands, bilateral proptosis with positive lid lag and retraction. Her thyroid gland was diffusely enlarged, firm and smooth with no palpable cervical lymph nodes. Erythrocyte sedimentation rate was 34 mm/hr, chest x-ray was normal, thyroid stimulating hormone (TSH) 0.005 U/ml (normal range 0.27 - 4.2), free thyroxine (T4), 70.95 ng/dl (normal range 12 - 22), TSH receptors antibodies 136 (normal range less than 1.8 IU/L). Thyroid ultrasound showed an enlarged hypervascular gland with bilateral cysts of which the largest one was 3.8 × 2.3 mm with one focal calcification in the cyst [Figure 1]. A diagnosis of Graves’ disease was made. The patient was started on antithyroid medications. She became pregnant soon after diagnosis, and during her pregnancy, she required high doses of antithyroid medication to control her hyperthyroid state. After delivery, she underwent a near total thyroidectomy. The histopathology of the thyroid gland revealed caseating granulomatous thyroiditis, giant Langhans cells and a heavy infiltration of lymphocytes in a background of a multinodular goiter, which was highly suggestive of tuberculosis (TB) [Figure 2]; and incidentally, multifocal papillary microcarcinoma with a maximum size 0.7 cm [Figure 3] was also detected. The granulomas were negative for acid-fast-bacilli (AFB) on a Ziel-Neelsen’s (ZN) stain and a specimen taken from thyroid tissue for polymerase chain reaction (PCR) to detect Mycobacterium (MTB) complex was also negative. The patient was started on a nine months course of antituberculous treatment and she did well.
In recent years, the incidence of extrapulmonary TB has been showing a progressive increase, thyroid involvement is extremely rare. The prevalence of thyroid TB varies from 0.1 - 0.6% in histologically diagnosed specimens. The exact reasons for this rarity of thyroid TB is unknown. The rarity of this disease may be attributed to various factors including bactericidal properties of colloid material and high thyroid blood flow. Tuberculosis infection of thyroid may present first in the thyroid or appear secondary to a tuberculous process elsewhere. Granulomatous lesions are not pathognomonic of TB, as they may be seen in sarcoidosis and subacute thyroiditis. The caseating necrosis, giant Langhans cells and lymphocyte infiltration, if present, as in our case, confirms the diagnosis of TB. The presence of AFB in the specimen consolidates the diagnosis, but MTB is rarely seen by the ZN stain of thyroid specimens. Detection of MTB, DNA from the thyroid specimen by PCR, is used in recent years as useful tool to provide an alternative for rapid diagnosis of thyroid TB in AFB negative cases. However, PCR for MTB may be positive in 55% of cases. It is quite interesting to note in our patient that thyroid TB was seen with Graves’ disease and multifocal micropapillary carcinoma, which may be the first such case described in the literature. The coexistence of Graves’ disease with papillary carcinoma of thyroid is well-known and reported in several cases in the literature. In one study, 7.8% of surgically treated Graves’ disease thyroid specimens showed papillary thyroid carcinoma. The coexistence of papillary carcinoma and TB thyroid is extremely rare and a literature review revealed one case report.

Graves’ disease is a relatively common disease and multinodularity in the thyroid gland in Graves’ disease is not uncommon. In view of the existence of other pathologies, careful scrutiny of these nodules should be undertaken and suspicious nodules should be subjected to fine-needle-aspiration, and operated thyroid specimens of Graves’ disease should be carefully search for other coexistent pathologies like papillary carcinoma and TB, because of definitive treatment available for such coexisting pathological conditions.

REFERENCES


A rural medical college perspective for treating pulmonary and extrapulmonary tuberculosis in a hepatitis surface antigen (HBsAg) positive patient

Vinod Prabhu¹, Aslam Shivani¹, Avinash Patil¹, Vishrabda Pawar²

¹Departments of Surgery, ²Pathology, Bharati Medical College, Sangli, Maharashtra, India

ABSTRACT

Pulmonary tuberculosis (TB) still forms a challenge in developing countries due to various forms of presentation, in spite of efforts taken by governments, non-governmental organisations (NGOs) and medical staff. Extrapulmonary TB is about 5% of all cases of TB, out of which perianal lesions constitute about 0.7%. The presence of hepatitis B surface antigen (HBsAg) positive disease with tuberculosis poses a challenge from both diseases, as regards the dilemma of treating the tubercular lesion with respect to hepatitis B surface antigen (HBsAg) positivity because of the compounding hepatotoxicity of anti-tubercular drugs and complications of cirrhosis and hepatocellular carcinoma. This is further complicated by a tuberculin test negativity, which in turn indicates a diminished immune status. This case report discusses a case of pulmonary and extrapulmonary (perianal) tuberculosis in a HBsAg positive patient.

Keywords: Hepatitis B surface antigen, perianal tuberculosis, tuberculin test

INTRODUCTION

Pulmonary tuberculosis (TB) is a common disease in developing countries. Along with extrapulmonary TB, it assumes a disseminated form. This is aggravated by hepatitis B surface antigen (HBsAg) positivity which complicates the treatment. The patient needs to be monitored for deranged liver function while on drugs. Active surveillance is needed for these patients as they are at high risk of developing hepatocellular carcinoma and liver cirrhosis. This case attempts to discuss all these aspects.

CASE REPORT

The presenting case was of a 60-year-old non-alcoholic male patient complaining of an ulcer near his anal opening for two months, which was painless with a colourless discharge. It was not associated with loss of weight, appetite, fever, cough with expectoration, or changed bowel habit. After visiting various clinics, he presented to us with the non-healing ulcer.

On examination, he had an ulcer in the perianal region 5 × 4 cm in size with pale granulation, seropurulent discharge and undermined edges [Figure 1]. There was no past history of perianal fistula nor was there any internal opening palpable or visible on proctoscopy. His blood count was normal. Erythrocyte sedimentation rate was 30 mm/hr, human immunodeficiency virus (HIV) was negative, liver function tests revealed (HBsAg) positive and alanine aminotransferase (ALT) 81 IU/L. Abdominal sonography was normal. Due to economic constraints the patient was unwilling for a colonoscopic exam and computed tomography (CT) abdomen. The magnetic resonance imaging (MRI) of the perianal region showed a small blind fistulous tract from the floor of the ulcer towards the anal canal, tuberculin test...
(TT) was 0 mm at 48 and 72 hours with no induration. Edge biopsy of the ulcer revealed TB [Figure 2].

The chest x-ray showed a tuberculous infiltration and the sputum was positive. Treatment by directly observed treatment with a four drug regime was initiated.

**DISCUSSION**

TB is still a major health threat in the developing world as it still bears socioeconomic implications. Periorificial TB forms a small percentage of extrapulmonary TB and is rarely seen.[1] Pulmonary TB spreads to extrapulmonary sites like the perianal region due to swallowing of tuberculous infected sputum.[2] It can also occur as a result of hematogenous, lymphatic or direct spread of the disease. There are five types of perianal and anal tuberculous involvement, ulcerative, verrucous, lupoid and fissure-in-ano are all documented.[3]

Fistula is the most frequent lesion of anorectal and perianal TB and should be suspected in long standing and recurrent fistulae. Tuberculous fistulae are usually multiple, with pain, local swelling and anal discharge.[4]

This case was compounded by the fact that in spite of HIV negative status the TT was 0 mm indicating a very low level of cell mediated immunity and the patient was HBsAg positive posing a secondary challenge. There is a known increase in incidence of pulmonary TB in HBsAg positive cases.[5] Here, the ALT levels need to be examined because these levels decide whether the patient is to be categorised in active or inactive group, as the inactive group which has a normal ALT level (<40 IU/L) needs no active management and are labelled as Incidentally Detected Asymptomatic HBsAg Positive Subjects.[6] However, detecting levels of hepatitis B e antigen (HBeAg) is more indicative along with ALT levels but is cost restrictive in developing countries. The two important complications in HBsAg positive cases are hepatocellular carcinoma (HCC) and cirrhosis. A higher rate of cirrhosis occurs in HBeAg negative patients with raised ALT than HBeAg positive patients. Furthermore, HBeAg status does not predict the risk of HCC. Due to this uncertainty, ALT monitoring and regular follow-up form the mainstay of management in a developing country. This case had ALT levels >40 and hence required close follow-up.

The use of anti-tuberculous drugs also poses a challenge in HBsAg cases. Normal ALT levels permit the use of drugs with minimum complications as compared to raised ALT levels because this altered liver function makes hepatotoxicity of drugs a common complication that requires frequent monitoring of liver function when on anti-tuberculous treatment.[7]

Furthermore, the TT was negative indicating a low cell-mediated immunity. Patients with low cell-mediated immunity have been shown to have high carrier rates of HBsAg.[8] It is not unusual to have a negative TT as it indicates either a recent infection or an overwhelming infection. This case has been proven histologically and sputum positive for active infection and hence TT loses its significance but the reason for discussing this aspect of TT arises in latent tuberculosis wherein two-step testing is required. It has also been observed that TT reaction decreases with time even after bacille Calmette-Guerin immunization. If a second correctly administered and interpreted skin test is negative, then the individual does not have a TB infection, but a positive test indicates TB infection, the first test acting as an immunostimulant.
CONCLUSION

In cases of pulmonary and extrapulmonary TB occurring simultaneously and complicated by asymptomatic HBsAg positive cases, it is advisable to quantify enzyme ALT levels and start Anti Kochs Treatment (AKT) drugs, monitoring liver function every month to detect early hepatotoxicity in patients having raised ALT (> 40 IU/L). These patients need to be followed-up regularly for development of cirrhosis and HCC.

REFERENCES


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Expected benefits of clinical practice guidelines: Factors affecting their adherence and methods of implementation and dissemination

Saja H Almazrou Mazrou
Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

ABSTRACT
The aim of this paper was to determine the expected benefits of clinical practice guideline implementation, discuss the criteria of a successful clinical guideline, explore the common factors that affect the adherence to their implementation and finally to identify the widely used guidelines dissemination methods.

Keywords: Adherence, clinical practice guidelines, implementation

INTRODUCTION
A search for ‘clinical guidelines’ on the World Wide Web at this time will result in hundreds of thousands of hits. Even allowing for many duplicates, there is clearly a massive worldwide interest in writing and publishing ‘top practice’ clinical guidelines, motivated by the aim of encouraging evidence-based clinical practice. Clear there is benefit in knowing whether a recommendation is based on the results of a well-designed, unbiased study published in a high ranking, peer-reviewed, scientific journal. With this information, a physician faced with a clinical decision can decide whether to follow a particular recommendation based, in part, on the assigned strength of the evidence on which the recommendation was made. The development of clinical practice guidelines (CPG) ensuring the appropriate use of evidence represents one of the core functions of many well recognized national and international originations specialized in many healthcare-related issues. CPG are defined as ‘systematically developed statements to assist practitioners and patient decisions about appropriate healthcare for specific clinical circumstances’.

EXPECTED BENEFITS FROM CLINICAL PRACTICE GUIDELINES IMPLEMENTATION
CPG are considered as one of the most influential and effective tools for the promotion of evidence-based medicine (EBM). CPG are being touted as a cure for the tension between healthcare cost and quality. Rather than being just a means of controlling clinicians, guidelines also offer the chance to improve the quality of care by reducing practice variation and adherence to standards of good care. Guidelines can be used in a wide range of settings to promote effective and efficient healthcare – for example to guide the introduction of new procedures or services, promote effective healthcare in primary or secondary care settings, encourage the adoption of cost-effective interventions and improve the timing and processes of the discharge of patients. Effective implementation of clinical guidelines have also been found to improve clinical outcomes, reduce the length of hospitalization, referral, emergency department (ED) visits, frequency of monitoring and cost are discussed below.
Clinical outcomes

Improvement of clinical outcomes by effective utilization of practice guidelines have been studied in many disease states such as asthma, pneumonia and psychiatric disorders. A recent study carried out in Japan to investigate the variations in the clinical efficacy and drug cost following the introduction of the Asthma Prevention and Management Guidelines (APMG), by reviewing the medical charts of 50 adults outpatients treated continuously for asthma. After the introduction of guidelines, distribution of asthma symptom severity varied significantly ($P < 0.0001$) and fewer patients were recognized as having more severe asthma symptoms. Significantly, more patients with severe asthma symptoms were detected in the physicians’ non-compliant group than in the compliant group ($P < 0.0001$). The number of patients prescribed with oral corticosteroids, long-acting beta2-agonists containing patches, long-acting oral beta2-agonists, short-acting inhaled beta2-agonists, sustained-released theophylline and leukotriene receptor antagonists decreased after the introduction of the guidelines.[7]

Another study was carried out in Australia to study the effect multifaceted interventions such as small workshops and locally adopted guidelines on health outcomes of children and adolescents with asthma. The adolescents reported an improvement in quality of life subscale score ‘positive effects’ (mean difference = 2.64, $P = 0.01$).[8] Although adherence to clinical guidelines have been reported to improve clinical outcomes in asthma, the study published in BMJ oppose these findings. Eccles et al., evaluated the use of a computerized support system for decision making for implementing evidence-based clinical guidelines for the management of asthma and angina in adults in primary care. Assessing adherence to the guidelines was based on review of case notes and patient reported outcomes. The results found that the computerized decision support system had no significant effect on consultation rates, process of care measures (including prescribing), or any patient reported outcomes for either condition. This was probably due to low levels of use of the software, despite the system being optimized as far as technically possible. Even if the technical problems of producing a system that fully supports the management of chronic disease were solved, there remains the challenge of integrating the systems into clinical encounters where busy practitioners manage patients with complex, multiple conditions.[9] The clinical outcomes were assessed in the treatment of pneumonia, a review found that implementation of guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia decreases the rate of initial inappropriate antibiotic treatment and decreased 14-day mortality.[10] However, other reviews concluded that guidelines implementation can improve outcomes. To achieve this goal, guidelines should be adapted to local microbiology, accurately predict ventilator associated pneumonia pathogens and help physicians to administer the most appropriate empirical antimicrobial therapy.[11] Psychiatric disorders such as depression and anxiety have been investigated in terms of clinical improvement after guidelines adoption. A study carried out by Hepner et al., to estimate how frequently specific guideline recommendations are followed and to assess whether following guideline recommendations is linked to improved depression outcomes. Greater adherence to practice guidelines predicted significantly fewer depressive symptoms.[12] In contrast, a review published by Baldwin et al., which include a number of RCTs in anxiety, panic disorders and depression, found that introducing guidelines does not significantly improve the clinical outcomes. The disappointing nature of these findings may be attributed to many reasons such as difficulty in diagnosing psychiatric disorders. In addition, it was noted that many physicians doubt the effectiveness of anti-depressants.[13]

Hospitalization and ED visits

The impact of adherence to CPG on hospitalization have been studied by Sloan et al. The research objective was to study the discrepancy between actual and recommended rates of use among several measures of screening for complications of diabetes in a national longitudinal sample, the correlations among measures of adherence, and whether or not higher rates of adherence reduce hospitalizations for complications of diabetes. The results found that increased rates of adherence were observed for HbA1c and lipid testing over the observation period. Higher use was associated with significantly lower rates of hospitalization for vascular, renal and other complications of diabetes.[14] Furthermore, adherence to guidelines not only reduces hospitalization but also reduces the emergency and outpatient visits for children with asthma. This has also been concluded by Cloutier et al.; their study aimed to determine whether adherence to the guidelines by primary care providers (PCPs) decreases medical services utilization in low-income, minority children. After enrolment in easy breathing, provider adherence to the National Asthma Education and Prevention Program (NAEPP) guidelines, children with asthma experienced a 35% decrease in overall hospitalization rates ($P < 0.006$), a 27% decrease in asthma ED visits ($P < 0.01$) and a 19% decrease in outpatient visits ($P < 0.0001$).[15]
**Referrals**

In a recent systematic review, assessing the effectiveness of guidelines for referral for elective surgical evaluation, found that guidelines for elective surgical referral can improve appropriateness of care by improving pre-referral investigation and treatment.\(^{[16]}\) An audit was undertaken by Hill et al., to assess how appropriate referrals were just before and after spreading of the guidelines and was repeated 2 years later to determine whether they had made any substantial impact. The results revealed a 40% increase in the number of appropriate referrals immediately after introduction of the guidelines, but this was not sustained 2 years later. The study concluded that there is a need for continued general practitioner education support referral guidelines.\(^{[17]}\)

**Use of diagnostic tests**

Other expected benefits of using practice guidelines are the reduction in the frequency of laboratory monitoring. Using a retrospective chart review, Gentile et al., compared the use of chest radiography (CXR) and arterial blood gas testing (ABG) before and after initiation of specific ordering guidelines, after guideline initiation, there was a 55% reduction in the number of chest radiographs. Of the patients who did not have a chest x-ray in the ED, none had an abnormal chest x-ray obtained after admission or if they returned to the ED within 72 hours. There was a 57% reduction in the number of ABGs. Although patients with abnormal ABGs had an apparent indication for testing, all of the ABGs for which no indication could be found were normal. A protocol containing criteria for obtaining chest x-rays and ABG testing can reduce the use of diagnostic testing, thereby improving ED efficiency without adversely impacting patient care.\(^{[18]}\)

**Cost**

Many studies also suggest that successful implementation of CPG can save cost. A study was undertaken by Prat et al., to assess the impact of clinical guidelines to improve appropriate use of routine laboratory tests and bedside chest radiographs in a 15 bed medical intensive care unit. They found that an overall 300,000 Euros intensive care unit (ICU) cost reduction was directly related to the protocol implementation.\(^{[19]}\) Baer et al., discovered that electronic neonatal intensive care unit (NICU) transfusion ordering and monitoring system as part of a new program to improve compliance with transfusion guidelines, resulted in an annual decrease of $780,074 in blood bank charges.\(^{[20]}\) Recent research in Japan investigated the variations in the clinical efficacy and drug cost following the introduction of the APMG, the results found that the total annual drug cost per patient decreased significantly by an average of 16,259 Yen, US $165 (\(P = 0.006\)).\(^{[21]}\) Although many studies provide evidence that effective implementation of practice guidelines can save cost, there are some contradictory findings discussed by McColl et al., which states that ‘clinical guidelines will be cost effective only if the resources spent to develop and disseminate them are justified by reductions in healthcare expenditure or improvements in patients’ outcomes. There is very little evidence so far that guidelines are helpful in terms of cost containment’.\(^{[22]}\) Fortunately, more studies have been carried out in the past decade to support that following practice guidelines is cost effective in many disease states as discussed earlier.

**SUCCESSFUL CLINICAL GUIDELINES AND UPDATING**

There are many methods used in the development of guidelines, including explicit approach, consensus conference/working party, synthetic method and health economics.\(^{[23]}\)

The development of a good guideline requires the active participation of key clinical staff, a systematic review of the scientific evidence, the linking of that evidence to the guideline recommendations and careful attention to other quality criteria such as clarity and clinical flexibility. A successful clinical guideline should correctly interpret the available evidence in order that, when followed, guidelines lead to improvements in health. And when given the same evidence, another guideline group would produce similar recommendations. In the same clinical circumstances, another health professional would apply these guidelines similarly. Guidelines should be representative of all key disciplines and interests (including patients), clinically applicable with a clear definition of the target population and identify where exceptions to the recommendations lie. Furthermore, it must be clearly expressed using precise definitions, unambiguous language, a user-friendly format and clear links of recommendations to the available evidence. Finally, the guidelines should state when, how and by whom they are to be reviewed. Significant resources are being expended internationally on the progress of CPG.\(^{[6]}\)

Clinical guidelines require updating. The majority of recommendations can become outdated due to changes in research findings and recently available diagnostic or therapeutic interventions. In general, guidelines should be re-assessed for validity every 3 years. In rapidly evolving fields, for example acquired immunodeficiency syndrome (AIDS) or colonic cancer, yearly review is necessary.\(^{[23]}\)

Although consensus is increasing about methods for developing evidence-based guidelines, still less
consideration has been paid to the process for assessing when guidelines should be updated. There are some situations that require clinical guidelines updating such as: (i) Changes in evidence on the existing benefits and harm of interventions. (ii) New information about the magnitude of benefits and harm may make the pre-existing guideline invalid. (iii) Changes in outcomes considered important. (iv) New evidence may identify an important outcome that was previously unappreciated or unrecognized. (v) Quality of life, for example an end point often not considered in earlier research and guidelines, is receiving increasing recognition as an important outcome of healthcare. (vi) Changes in available interventions since the development of a guideline, new preventive, diagnostic or treatment interventions may have emerged to complement or supersede other interventions. (vii) Changes in evidence that current practice is optimal, guidelines are developed to help narrow the gap between ideal and current clinical practice. This gap could narrow over time to the point that a guideline is no longer needed. (viii) Changes in values placed on outcomes, the values that individuals or society place on different outcomes may change over time. Economic issues, for example have received little attention in most guidelines but will be considered explicitly in guidelines developed by the UK National Institute for Clinical Excellence. (ix) Changes in resources available for healthcare guidelines may need to be updated to permit increased delivery of services if the level of available resources increase over time.[24]

**FACTORS AFFECTING GUIDELINES IMPLEMENTATION**

Increasing efforts are being taken to translate guidelines into clinical practice, but many factors affect physicians from adopting them. There is a growing literature that explores the barriers to the implementation of clinical guidelines in healthcare, and that identifies effective strategies for translating research into practice. Although most guidelines are useful tools to provide the busy clinician with up-to-date information, physicians may regard guidelines to be unrealistic, and some may even consider guidelines to be a challenge to their autonomy. A further hazard of guidelines is that they may inhibit research or innovation.[22] These barriers can be classified into organizational and resources, physicians and guidelines-related factors.

**ORGANIZATIONAL AND RESOURCE RELATED FACTORS**

Effective organizational structure with strong leadership and a powerful learning culture were found to be important facilitating factors in implementing CPG. Additionally, supporting guidelines adoption by the department chief and mandating the guidelines implementation with a multi-disciplinary team is also considered to be successful modalities in working with guidelines.

Lack of financial resources was also raised as an essential issue that prevents the progress of implementation work. Finally, consistent evaluation of the quality of the care provided by giving feedback on the organization’s performance will ensure the durability and efficiency of implementation strategies.[25]

**PHYSICIANS’ RELATED FACTORS**

The degree to which clinicians adhere to guidelines has been the subject of numerous studies, usually based on surveys of real world practice. Studies found that knowledge, attitude and behaviour are considered the main factors that affect physicians’ adherence and will be discussed as follows.

**Knowledge**

Although CPG have been promoted widely, there is considerable concern that physicians have not incorporated them into their practice. Knowledge such as lack of familiarity and awareness, volume overload, time needed to stay informed and guideline accessibility are important in modifying physician practice patterns.[26]

Forsner et al., addressed other physician-related barriers such as lack of research skills and specialized training. [25] Lacking these skills may lead to inability to find the most appropriate resources for evidence-based guidelines.

**Attitude**

Physician attitude about practice guideline is another barrier to guideline adherence. Lack of agreement and confidence with specific guidelines, that explain that most individual doctors may not agree with guidelines issued by their own peers, leading them to choose a different course of treatment, however, many doctors have seen that a specific guideline may be too rigid to apply. Also lack of outcome expectancy, self-efficacy and motivation to implement practice guidelines in addition to habit and routines have also been found to hinder effective practice guideline implementation.

**Behaviour**

This is considered as an external barrier, which includes patient, guideline and environmental-related factors.[26] Francke et al., found that patient-related characteristics may include the fact that some patients
perceive no need for guideline recommendations or resistance towards the guidelines recommendations as a factor negatively affecting the adoption of clinical guidelines.[27] The guideline factors such as the presence of contradictory guidelines and environmental factors including lack of time, resources and reimbursement. Organizational constraints and perceived increase in malpractice liability are the most important external barriers that affect guidelines implementation.[28]

GUIDELINE-RELATED FACTORS

CPG should be compatible with existing values among the target group and not be too controversial. They should not demand too much change to existing routines and be defined precisely, with specific advice on actions and decisions in different cases. They should be compatible with current values and routines. Indeed, some recommendations probably expressed what general practitioners were already prepared to do. The scientific basis of the recommendation is also important. Recommendations were more adhered to when an explicit description of the scientific evidence was available and the evidence was straightforward and not conflicting. The perceived consequences for doctors and practice management matter. A recommendation was used less when compliance affected the organization of and staff in practices, when it demanded extra resources or acquisition of new knowledge and skills, or when it provoked negative reactions in patients.[28]

In a recent meta-analysis published in 2008, it suggested that the most frequently described guideline characteristic concerns complexity. Guidelines that are easy to understand, can easily be tried out and do not require specific resources have a greater chance of being used.[27]

PROFESSIONAL DISSEMINATION AND IMPLEMENTATION

Although barriers exist, many dissemination and implementation strategies aim to improve adherence to CPG. The most common strategies are listed below:

Distribution of educational materials in paper or electronic versions, small laminated cards, posters available where care was delivered and short versions of the guidelines posted. Furthermore, reminders are being utilized in guidelines implementation as well. Reminder is a patient- or encounter-specific information, provided verbally, on paper or on a computer screen, which is designed or intended to prompt a health professional to recall information. This would usually be encountered through their general education, in the medical records or through interactions with peers, and so remind them to perform or avoid some action to aid individual patient care. Computer-aided decision support and drugs dosage are included.[29] Unlike educational materials, reminders are patient specific and can be electronic pop-ups that appear on the screen when a chart is opened or a paper reminder placed in the chart, such as a pharmacist note advising clinicians that a patient requires blood tests to ensure toxicity is not an issue with a drug, or that a particular medication may be better for a patient based on best evidence. Reminders are more targeted and less passive than general educational materials.[30]

Other widely used methods are audit and feedback by giving a summary of clinical performance of healthcare over a specified period. This summary may also have included recommendations for clinical action. The information may have been obtained from many resources such as medical records, computerized databases or observations from patients.[29] Audit and feedback could be provided to individuals or the team as a whole. By understanding how close or not to targets team members were is an approach to either celebrate success, or examine issues that may be preventing adequate adherence to a guideline.[30]

Additionally, educational outreach visits by using a trained person or team of healthcare professionals from another institution or organisation who met with providers in their practice settings to give information with the intent of changing the provider’s practice. The information given may have included feedback on the performance of the provider(s). Many other less common strategies were used in guidelines implementation such as local opinion leaders and the consensus process, patient mediated intervention, marketing and mass media. However, there is an imperfect evidence base to support decisions about which guideline dissemination and implementation strategies are likely to be efficient under different circumstances. Decision makers need to use considerable judgment about how best to use the limited resources they have for clinical governance and related activities to maximize population benefits.[29] Technology plays an important role in the implementation and dissemination of practice guidelines but further studies are needed to demonstrate their effectiveness and cost implication. A study aimed at examining whether Palm Prevention, a free software tool for Palm OS personal digital assistants (PDAs) that provides quick access to preventive guidelines in a patient-specific manner at the point of care, improved adherence to five preventive measures in primary care. The results suggested that PDAs are
useful in improving preventive care and facilitating translation of knowledge into practice. This was particularly apparent with newer guidelines.\(^{[31]}\)

Furthermore, educational games are of growing interest and have the potential to improve adherence to practice guidelines. Research was carried out to develop an educational game to teach clinical guidelines in internal medicine residency programs and to evaluate its feasibility and acceptability. The Guide-O-Game\(^{©}\) is a multimedia interactive tool in the format of a TV game show with questions based on recommendations of practice guidelines. The study findings suggest that an educational game is feasible and acceptable. Future work should evaluate its impact on educational outcomes.\(^{[32]}\)

**REFERENCES**


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Status of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in the Kingdom of Saudi Arabia

Fahad Al Rabiah
Department of Medicine, Infectious Diseases Section, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, Member in National Committee of Infectious Diseases, Ministry of Health, Riyadh, Saudi Arabia

ABSTRACT
In September 2012, a case of novel coronavirus (CoV) infection was reported in Saudi Arabia. It is caused by a CoV called Middle East Respiratory Syndrome (MERS). Eight countries have reported the virus so far, with most of the reported cases from Saudi Arabia. Fatality rate is about 44% and most people who have been confirmed to have MERS-CoV developed severe acute respiratory illness. There is very limited information on transmission, severity and clinical impact with only small number of cases reported so far. However, the virus has not shown to spread in sustained way in communities. There is no available vaccine or proven treatment for this novel virus; however, there are several treatment protocols under trail. Healthcare is provided to infected individuals by alleviating symptoms and treating its complications; nevertheless the situation is still evolving.

Keywords: Coronavirus, Middle East Respiratory Syndrome Coronavirus, Saudi Arabia, severe acute respiratory syndrome

In 2003, severe acute respiratory syndrome (SARS), a new disease caused by a previously unknown coronavirus caused major worldwide alarm and concern. Almost 10 years later in 2012, the discovery of another novel strain of SARS-like coronavirus is causing unusually severe pneumonia in a majority of infected patients.[1,2] This novel coronavirus has been named Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Since then, MERS-CoV has been identified as the cause of pneumonia in patients in Saudi Arabia, Qatar, Jordan, the United Kingdom, Germany, France, Tunisia and Italy.[2,4]

Since the first reported Saudi case of MERS-CoV, the Saudi Ministry of Health mandated that all patients with respiratory illnesses needing admission to intensive care should be tested for the virus using any available clinical specimen.

Respiratory viruses are an emerging threat to global health security and have led to worldwide epidemics with substantial morbidity, mortality and economic consequences. MERS-CoV is a member of the coronavirus family, Coronaviridae family, a group of large, enveloped single-stranded RNA viruses that cause a range of infections in mammalian and avian hosts. Coronaviruses are responsible for one-third of all cases of the common cold. Human coronaviruses usually cause mild-to-moderate upper-respiratory tract illnesses of short duration. MERS-CoV is considered distinct from the coronavirus responsible for the SARS-CoV, which is a virulent, transmissible human pathogen that first emerged in southern China in the fall of 2002.[9]

There are currently no vaccines available to protect against human coronavirus infections.
The origin of MERS-CoV virus remains unidentified. Many of the important facts about this virus are still unknown, particularly where it comes from and how it spreads. However, although it has a worrying high mortality rate, most of those who have died already had pre-existing conditions.\(^5\)\(^-\)\(^7\)

Molecular investigation indicated that bats in Saudi Arabia are infected with several alpha and beta coronaviruses. Virus from one bat recently showed 100% nucleotide identity to the virus from the human index case patient from Saudi Arabia.\(^10\) Bats might play a role in human infection.\(^10,\)\(^11\)

Early scientific evidence suggests that the virus might already be widespread in animals but much about this virus remains to be understood. Animals might play role as intermediate host for MERS-CoV transmission to humans. Most important of all is whether infection can be sustained through human-to-human transmission.\(^12,\)\(^13\)

All cases originated from, or had a history of travel to, the Middle East, except for two secondary cases in the UK, two in Tunisia and one in France. A large cluster \((23)\) of cases has been documented in one hospital in Saudi Arabia, and another is suspected on the basis of a retrospective analysis of samples kept after an outbreak of respiratory disease in a Jordanian hospital in April 2012.\(^12\)

Whereas as yet, an unidentified animal reservoir might have caused the initial outbreaks by introducing the virus into the human population, the occurrence of clusters, whether in the community or in hospitals, is a worrying development, because it might result from adaptation of the virus to inter-human transmission.\(^14,\)\(^15\)

Most patients with MERS-CoV infection have been severely ill with pneumonia and acute respiratory distress syndrome, and some have had acute kidney injury. Other clinical manifestations that have been reported are gastrointestinal symptoms (anorexia, abdominal pain, diarrhoea), pericarditis and disseminated intravascular coagulation.\(^5,\)\(^12,\)\(^13\)

In review of 47 cases of MERS-CoV in Saudi Arabia, the case fatality rate rose with increasing age. Most patients \((96%)\) had comorbid medical conditions including diabetes mellitus, cardiac and renal diseases.\(^5\)

As of 30 September 2013, a total of 136 cases of human MERS-CoV infection with 60 deaths have been reported to the World Health Organisation (WHO). Of those, 114 cases had been reported from Saudi Arabia with 49 deaths.\(^16\)

Routine MERS-CoV testing of all patients with severe pneumonia is now on-going in Saudi Arabia. Serologic testing of close contacts of patients with this disease will help to define local transmission and risk factors. Laboratory testing for MERS-CoV remains a challenge. Validated serologic assays are not yet commercially available, and this may have limited the identification of cases. WHO and Centers for Disease Control and Prevention recommend that lower respiratory tract specimens should be the first priority for collection and real time reverse-transcriptase polymerase chain reaction (rRT-PCR).\(^17\)\(^-\)\(^19\) It seems prudent to conclude that one cannot reliably rule out MERS-CoV disease on the basis of a single negative test when a patient presents with the appropriate clinical syndrome and epidemiologic exposure. There is evidence that repeat testing of sputum or bronchoalveolar-lavage fluid is of value in improving diagnostic accuracy.\(^20,\)\(^21\)

The WHO does not recommend either special screening for MERS-CoV at points of entry or the application of any travel or trade restrictions.\(^22\) The Saudi Ministry of Health recommends that elderly \((aged above 65 years)\) and those with chronic diseases \((e.g.\) heart disease, kidney disease, respiratory disease, diabetes) and pilgrims with immune deficiency \((congenital and acquired),\) malignancy and terminal illnesses, pregnant women and children \((under 12)\) coming for Hajj and Umrah this year, to postpone the performance of the Hajj and Umrah for their own safety.\(^23\)

Although current data on MERS-CoV infections are biased by high case fatality in admitted patients with medical co-morbidities, since 15 June 2013, the Saudi Ministry of Health has further reported MERS-CoV infections in at least 16 asymptomatic individuals after screening contacts of confirmed MERS-CoV cases.\(^24\)

Population-based antibody testing will help to establish the extent of MERS-CoV infection, instead of only seeing the tip of the iceberg represented by cases admitted. As of today, data indicate that MERS-CoV does not appear to be as readily transmissible among humans; however, continued risk assessment, surveillance and vigilance by all countries are required. The public health communities in all countries must be aware of the public health risk associated with this MERS-CoV virus. It is not clear yet how far this virus might spread and nobody knows what impact it may have on global health.

**REFERENCES**


8. Gullan A. Two cases of novel coronavirus are confirmed in France. BMJ 2013;346:f3114.


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