Points of interest

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Antimicrobial Resistance News

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ECMMID Report

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Syphilis in the Northern Cape

17th ICID
On 27th May 2015, the World Health Assembly (above), adopted the World Health Organization Global Action Plan (GAP) on Antimicrobial Resistance. This marked the culmination of a year of diplomacy and consultation by the tripartite alliance (WHO, OIE and FAO). Member States are now mandated to produce a national strategy for combating Antimicrobial Resistance by May 2017.

The GAP agenda will be taken forward as part of the Global Health Security Agenda (GHSA), whose Prevent-1 Action Package focuses on Antimicrobial Resistance. A side meeting of lead and contributing countries to Prevent-1 was held at the WHA, where the 2015 work package was agreed. Collaboration is the name of the game, and South Africa is taking forward partnerships to help strengthen our response.

One week after the GAP was adopted, the Uppsala Health Summit 2015 ‘A World Without Antibiotics’ took place in Uppsala, Sweden. The pre-conference report can be accessed at www.uppsalahealthsummit.se/wp-content/uploads/2015/05/UJS-Pre-Conf-Report-2015.pdf.
The Human Microbiome at ECCMID 2015 - Samantha Potgeiter

Two colleges and I had the pleasure of attending the European Congress for Clinical Microbiology and Infectious Diseases (ECCMID) in Copenhagen in April this year. Copenhagen is a fascinating city – where the number of bicycles reportedly outnumber the 1.9 million metropolitan inhabitants. In fact there are 5 times as many bicycles as motor cars in the Danish capital!

The congress itself was also fascinating. I found it so interesting to attend an ID congress where very little was said about HIV and TB – the two topics that dominate most local platforms. Most sessions centered on multi-drug resistant organisms and antibiotic stewardship, new drug development pipelines, better and faster fungal diagnostics, and infections in the critically ill and neutropenic populations. There was also a lot said about a topic that up until now had only been on the “fringe of my ID radar” – ‘The Human Microbiome’.

The importance of the gut microbiome in the pathogenesis of Clostridium difficile infection has long been documented, as has the success of fecal transplant for treatment of recurrent C. diff disease. But what has up until now escaped my attention is the extreme importance that the human microbiome plays in health and disease in general.

The human microbiome is the collection of micro-organisms living in association with the human body. The statistics are just so interesting: There are approximately 10 times the number of bacteria in the human microbiome than there are human cells – accounting for about 1-3% of our body mass. Microbial genes outnumber human genes by a ratio of 100:1. Referred to as “The Other Genome” -these organisms have tremendous potential to affect our physiology. They are involved in our metabolic and immune function, and obviously play an important role in protection against pathogens. It is interesting to consider that the human genome is static and cannot be manipulated in disease settings whereas the microbiome could possibly be.

The Human Microbiome Project - started in 2008 - is dedicated to the comprehensive characterization of the human microbiome and analysis of its role in human health and disease. Many microbial constituents of the microbiome cannot be cultured and the science of metagenomics has enabled a much better understanding of the extremely diverse microbiome composition. A large amount of research is being done in this field and novel ideas about manipulating the microbiome - both in humans to treat disease and in animals to increase productivity in livestock - are being investigated. Many factors influence the diversity of the microbiome – Probiotics and prebiotics (generally in a positive way) and of course antibiotics (in a negative way). But other factors such as diet, lifestyle and exercise have also been shown to play an important role.
An interesting session at ECCMID was dedicated to the "Pros and Cons of Manipulating the Microbiome" (http://www.eccmidlive.org/resources/benefits-of-microbiome-manipulation-in-reducing-resistance). Mary-Claire Roghmann, Professor in Epidemiology and Public Health and Medicine from the University of Maryland in the US gave a fantastic lecture where she outlined the possibilities of manipulating the gut microbiome to eradicate colonization with drug resistant organisms. Studies in mice have shown that fecal transplant has been successful in eradicating VRE colonization. In a paper titled: “Use of stool transplant to clear fecal colonization with Carbapenem-Resistant Enterobacteriaceae (CRE)” – the authors Abigail Freedman and Stephen Eppes outline how they used faecal transplant to treat a young girl who had repeated severe CRE infections over a period of about 13 months, after receiving prior antibiotics for a mastoiditis. After a donor fecal transplant (from the patients younger brother) no further stool samples cultured CRE during a year and a half follow up period and the patient had no further documented infections. This represents a very interesting proof of concept - that faecal transplant may have a role to play in the treatment of patients colonized with multidrug resistant organisms. A fantastic thought in these dark days of "Bad Bugs, no Drugs" in which we live.

Stephen Harbarth from the University Hospital of Geneva spoke about the unintended consequences of manipulating the microbiome (http://www.eccmidlive.org/resources/unintended-consequences-of-microbiome-manipulation-including-decolonization). He spoke about the well-known case of the 32yr old woman who was treated with faecal transplant for recurrent C. diff infection. She was cured of C. diff but gained 18.6kgs in the 18 months post-transplant. Obesity has been linked with phylum level changes in the gut microbiota, reduced bacterial diversity and altered bacterial gene representation. This case raises an interesting question: Could faecal transplant then be used to treat obesity? He also presented a wonderful paper where the authors outline how faecal transplant in mice resulted in behavioral changes. A timid species of mice were transplanted with faeces from a more "risk taking" species and vice versa. It was incredibly interesting to note that the timid mice became obviously more risk taking whilst the initially risk taking mice became noticeably and quantifiably more timid. I find this concept absolutely fascinating – that alterations in the gut microbiome may have the potential to affect behavior.

The study of the Human Microbiome is a fascinating science and I believe it may represent amazing treatment strategies for the future. I look forward to following the progress in this field.

**ECCMID 2015 - Theunis Avenant**

The 25th European Congress of Clinical Microbiology and Infectious Diseases was held in Copenhagen, Denmark at the end of April 2015. This annual congress has grown exponentially over the past few years with an estimated 10 000 delegates attending.

The Bella Centre in Copenhagen proved to be the ideal setting for such a prestigious conference, having previously hosted important events under the auspices of the International Olympic Committee, European Union, the World Bank, NATO and the United Nations.

A series of educational workshops, arranged in cooperation with ESCMID study groups and other organizations, preceded the conference. As with any conference of this size, the conference programme had to be studied in detail to select from the up to 11 parallel sessions. In addition there were 1427 posters and 1141 thousand e-posters to be picked from.
Apart from the now common use of Twitter and Facebook, the congress had a very efficient smartphone app that gave information about the programme and exhibition. It allowed for networking through XING, LinkedIn or Facebook. In addition the app could be used to ask questions to, or rate the presenter at the end of sessions.

Visiting Copenhagen in between sessions, one is struck by the friendly efficiency of its citizens, or... if not careful... struck by one of the multitude of bicycles roaming the streets. Copenhagen is world famous for its biking culture. It has been voted the ‘Best city for cyclists’ with over 390 kilometres of designated bike lanes. Renting a bike proved to be one of the best ways to explore the city during our stay.

Back to the conference. Marc Bonten from Utrecht presented the results of the adult pneumococcal polysaccharide vaccine (PCV) efficacy study. This study looked at the efficacy of PCV13 against pneumococcal community acquired pneumonia in adults 65 years or older. It concluded that PCV13 was effective in preventing vaccine type community acquired pneumonia and vaccine type pneumococcal disease in this age group. The efficacy persisted for 4 years.

In a keynote lecture titled "World Immunization Week 2015 – WHO perspectives on vaccines" Robb Butler addressed to issue of how to deal with hesitancy to vaccinating children. He emphasized that medical professionals should not fight fear with fear. Instead of instilling alarm for the ill effects of not immunizing, time should be utilized to build a trusting relationship and provide as much information as possible. A novel idea was that of immunization services being open at times when working parents can access it, something very few EPI managers might have thought of.

The travel medicine session again questioned the effectiveness of thermal scanning technology at airports in preventing the importation of serious diseases. Nick Beeching of the Liverpool School of Tropical Medicine also discussed aspects of severe respiratory infections during and after travel. MERS-CoV has so far given rise to very few travel-associated cases with no major events associated with the Hajj.

A detailed description of the management of a patient with Ebola from Germany lead to many questions regarding the ethics of spending enormous amounts of money on a single patients at a time when countries like Sierra Leone and Liberia were struggling to contain an epidemic.

Linos Vandekerckhove paid tribute to Joep Lange, a former president of the International AIDS Society, and Jacqueline van Tongeren. They were on board the MH17 flight, en route to the International AIDS Conference in Melbourne, when it was shot down in July 2014. In the memorial lecture that followed progress on the provision of low cost and generic antiretrovirals were discussed. The decline in the development of new drugs was raised as an issue of major concern.

As networking opportunity the 25th ECCMID congress again proved invaluable. The next chance will be from the 9th to the 12th of April 2016 in Istanbul, Turkey.
Diphtheria remains endemic in several parts of the world. After 1976, the incidence of diphtheria cases in Russia began to rise due to social upheaval, leading to a massive epidemic in both the Russian Federation and Ukraine. Thereafter outbreaks in Europe, with possible epidemiological links, were also reported [1]. In developing countries, outbreaks of diphtheria have been reported in Asia, Latin America and Africa [2,3,4]. In South Africa, a total of 351 cases were reported in the 1980s, which included 68 patients from an outbreak in Lesotho [5]. Thereafter, the incidence of diphtheria in South Africa decreased significantly, with only twenty-nine cases reported in the 1990s. Since 2000, only five isolated cases were reported, with the last being documented in 2009 by Liebenberg et al [6,7]. The sudden appearance of toxigenic diphtheria in KwaZulu-Natal is of major concern. This may represent a possible resurgence of this contagious and potentially fatal disease.

To date, there are ten confirmed cases of toxigenic diphtheria in KwaZulu-Natal, South Africa. These cases include eight paediatric patients and two adults and were from the eThekwini area, including Umhlazi and Chatsworth, as well as the Port Shepstone area.
Throat and tonsillar swabs were submitted to the microbiology laboratory for routine microscopy and culture for suspected diphtheria. Isolates grew as black pigmented colonies on selective Hoyles’ plates and were confirmed as *C. diphtheriae* by biochemical tests and Matrix Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF). All ten isolates were confirmed by a reference laboratory as toxin-producing, using the Elek test.

A multidisciplinary outbreak response was initiated following on the first case and thereafter for all subsequent cases. Home visits of all cases were conducted by the local Communicable Disease Control (CDC) team of the Health department with screening of all close contacts. Field investigation revealed that there was a possible link between the first two cases. It was noted that a number of mothers did not have the Road to Health Immunisation card. In light of these findings, a decision was made by the local health authorities to vaccinate as many children as possible in the affected areas by undertaking a ‘Catch-up’ immunization campaign. Public awareness regarding the importance of immunization, not only within the affected areas, but across all areas within the province of KwaZulu-Natal, was created. A memorandum to alert health care workers was distributed to all primary health care facilities and hospitals. Health education at a community level was also carried out in order to facilitate early recognition of possible diphtheria cases.

In countries with successful childhood immunisation programmes, diphtheria is a rare occurrence. Thus many clinicians have very little or no experience in the clinical diagnosis and management of this disease. Respiratory diphtheria classically presents as a membranous pharyngitis with fever and enlargement of the anterior cervical nodes, including soft tissue swelling resulting in a “bull neck” appearance [8]. The typical distinguishing feature of diphtheria is a whitish grey membrane which covers the tonsils, pharynx and nasal cavity and importantly bleeds on removal [9]. However, in previously vaccinated individuals, the presentation may be atypical with absence of the membrane resulting in further clinical diagnostic challenges. It is imperative for clinicians to consider other infections that may mimic diphtheria such as bacterial tonsillitis, of which the commonest cause is *Streptococcus pyogenes*; acute epiglottitis, infectious mononucleosis, Vincent’s angina and oral candidiasis [10].

The mainstay of therapy for diphtheria is the administration of diphtheria antitoxin, which is only effective when given early. This is attributed to the fact that the antitoxin only neutralizes free toxin and has no effect on bound toxin. Administration of antitoxin was not possible in the initial cases. Antitoxin is not manufactured in South Africa and currently suppliers and manufacturers are limited globally. In addition, South Africa does not stock diphtheria antitoxin and it can only be obtained via a case-by-case basis through an emergency Medicines Control Council (MCC) Section 21 application from Israel, India or Japan. Failure to administer antitoxin increases morbidity and mortality [11].

Although antitoxin remains the mainstay of therapy, the use of appropriate antibiotics and supportive care are an integral component of management. Antibiotics halt toxin production, limit the progression of disease and prevent transmission of the causative organism. Antibiotics used in the treatment of diphtheria include parenteral benzylpenicillin or erythromycin for 14 days. Other possible options include azithromycin and clarithromycin. Patients become non-infectious within 48 hours of appropriate treatment. However, it is recommended that two cultures be taken; 24 hours after completing therapy and 24 hours apart. If either culture is positive, a further 10 days’ treatment with parenteral penicillin or erythromycin or is recommended.

Infection control must be initiated promptly in order to prevent secondary transmission of *C. diphtheriae*. Diphtheria is a notifiable disease and all suspected cases must be reported to the Department of Health. All close contacts must be traced and managed appropriately. Close contacts include family
members and those directly exposed to oral secretions of the patient. Nasal and throat swabs must be obtained from all close contacts in order to exclude carriage of toxigenic \textit{C. diphtheriae}. In addition, prophylactic antibiotics, benzathine penicillin as a stat dose intramuscularly or oral erythromycin/azithromycin which must be administered for 7 and 5 days respectively. A booster vaccination appropriate for age should be given to all those who have not had a booster vaccination in the past year [12]. Three contacts (siblings) of one of the ten cases were found to be colonised with \textit{C. diphtheriae} and all these four children, including the case, had missed all their childhood immunization.

For as long as ease of access to both diphtheria antitoxin and rapid diagnostic methods for the confirmation of toxigenic \textit{C. diphtheriae} are not in place, diphtheria will remain a potential threat in both developing and developed countries.

\textbf{References}
1. European journal of epidemiology 11: 107-117

\textbf{Hand Hygiene}

We end this quarter with a wonderful feeling of people energetically scurrying to do as much as possible to celebrate World Hand Hygiene Day on the 5\textsuperscript{th} May, in real and meaningful ways.

There was a request from the South African Antibiotic Stewardship Programme (SAASP) working group that all hospitals take part in a hand hygiene relay on the 5\textsuperscript{th} of May. Suggested outcomes for the relay were many, and suggestions included: creating awareness through a fun activity [relay], demonstrating competency with correct handrub technique, measuring competence, and even possibly improve on the previous Guinness world record of 991 people in a single relay that was set by an Indian hospital in Jamshedpur on the 18\textsuperscript{th} of January 2015. \url{http://www.guinnessworldrecords.com/world-records/most-participants-in-a-hand-washing-relay}

Photos and video clips are available on the WHO site as well as on Twitter #safe HANDS
Health Organization (WHO) Hand Hygiene Campaign in order to “Turn Africa Orange” and as you can see from the map below, you have helped to make a significant difference!

African Region- SAVE LIVES: clean your hands

Help Us Turn Africa Orange

Feb 2014: 669 hospitals  April 2015: 801 hospitals

Well done to all those who have already registered and we implore those of you who have not yet done so, to please register at http://www.who.int/gpse/5May/register/en/ and assist in making Africa even more orange! http://www.who.int/gpse/5May/registration_update/en/

Fellow Africans, we need your help to SPREAD THE WORD!

Advanced Diploma in Infection Prevention and Control Nursing

The core competencies for an Advanced Diploma in Infection Prevention and Control Nursing (IPC) lie with the South African Nursing Council (SANC) and we are holding our breaths in eager anticipation to be given the green light to go ahead and develop the curriculum. Exciting times and news that we are hoping to share at the conference in November!

The following institutions currently offer diplomas in IPC, but none are recognised by SANC:
Stellenbosch University
University of the Witwatersrand
University of Pretoria

Ebola Virus Disease
ICSSA are actively involved in a work group led by Dr Louis Claasens for the development of guidelines and training material for Ebola Virus Disease (EVD).

(Contributions from Joy Cleghorn and Briette du Toit)
Quebec City was the host city of the 14th Congress of the International Society of Travel Medicine. Topics ranged from in-flight emergencies, the Ebola outbreak, malaria and malaria guidelines, Japanese encephalitis (JE) vaccine in the elderly to vaccines in the pipeline, vaccine refusal and the development of dengue vaccines.

**New vaccines:** There is good news as there are many vaccines in the pipeline which will result in the reduction of illness. And there will be a flood of vaccines in the next decade. These vaccines are directed as being curative – targeting autoimmune diseases, cancer and even fertility. In addition, changes in vaccine composition will lead to more effective vaccines – such as an attenuated JE vaccine, and new vaccines targeting enterovirus 71, Ebola vaccines and many old vaccines in a new format which will increase efficacy of the vaccines. The most rapid development is in China with the production of an attenuated JE vaccine and a new BCG vaccine.

**Yellow fever vaccine:** The efficacy of the yellow fever vaccine is considered to be life-long in immunocompetent individuals. What was not discussed is the period of validity in the elderly and those who are, for whatever reason, immunocompromised. This recommendation will come into effect on 1 June 2016.

**Dengue vaccines:** The live chimeric vaccine (sanofi) shows considerable promise. It is unlikely that this will be a travel vaccine as protection is better in those individuals who have previous exposure to the virus. After three doses, given six months apart, high titres against all serotypes are achieved. The overall efficacy is lowest for serotype 2 and higher for types 3 and 4. The efficacy against Dengue Haemorrhagic Fever is between 88 and 99% and 91% for severe disease. Efficacy also depends on previous exposure to dengue virus – those who were flavi virus negative the efficacy is only 35%. After 12 months the efficacy is around 60%.
Ebola: Three vaccines are in the clinical phase – all have shown 100% efficacy in non human primates.

Malaria: is always a hot topic. A question posed was whether guideline consensus could be achieved, and this seems unlikely. The fact that there are guidelines does not equate to what happens in the real world as compliance, no matter how well the instructions are given, always raises its head. None the less there can be agreement on the approach that should be adopted. New prophylactic drugs and diagnostics could transform the landscape but continued surveillance of travellers is critical.

The resurgence of malaria will occur if more is not done. This entails removal of the human reservoir as it is the presence of gametocytes in the asymptomatic person that leads to the ongoing presence of malaria. Interrupting transmission will not lead to eradication of malaria. Complete cure of the asymptomatic mother and father will save the life of the child.

SERCAP – single exposure radical cure and prophylaxis - is the proposed route. A single, fixed dose, combination tablet that eradicates the gametocytes and is toxic to the mosquito is what is currently being explored. Well, asymptomatic people must be treated during the dry season and one should not wait until the commencement of the rainy season before action is taken. Chemoprophylaxis for children during the rainy season is also necessary.

In-flight medical emergencies: Approximately 7% of in-flight medical emergencies will cause a flight diversion. Most are vaso vagal episodes (53%) followed by gastro-intestinal (8.9%) and cardiac causes (4.9%). The most common cause for dyspnoea is anxiety.

Diversion is costly – between $100 – 200,000 - and the indirect costs are high. More airlines are using a ground based medical support system (GBMS) to assist in assessing the emergency.

What is one’s duty as a medical practitioner, to respond to an emergency call on board a flight? The Good Samaritan Law is applicable.

A practical guide is of value:
- If one does respond, see it through.
- It is likely that proof of registration as a medical practitioner will be called for
- Request the emergency kit and the AED if available.
- Request to be connected to the GBMS
- Do not charge for services rendered
- If a death occurs, this is not reason to divert the flight.

Other topics included dealing with vaccine refusal and how this can be addressed was discussed – the key is to use a motivational interviewing model. Vaccine refusal when travel vaccines advised is somewhat different to refusal in the paediatric setting where issues (unfounded) such as deleterious effects of the vaccine are the main reason for declining vaccination by the parents.
Decline in Syphilis seroprevalence among females of reproductive age in Northern Cape Province

Contribution: Dr Ngormbu J. Ballah: South African Field Epidemiology Training Programme, National Institute for Communicable Diseases, National Health Laboratory Service.

Globally, nearly 2 million pregnant women are infected with syphilis yearly. In developing countries 3-15% of women of child-bearing age have syphilis. In 2007, the World Health Organization launched its initiative for the Global Elimination of Congenital Syphilis. Strengthening of current surveillance systems for syphilis is significant for tracking and monitoring disease burden. In South Africa, National Antenatal Sentinel HIV & Syphilis Prevalence Surveys (ANSUR) has been conducted annually to monitor syphilis seroprevalence among pregnant women. However, utilisation of electronic laboratory data for surveillance would be an appropriate approach to estimating syphilis burden. We described trends in syphilis seroprevalence in women of reproductive age in the Northern Cape Province between 2003 and 2012 and compared findings from ANSUR with those computed from the National Health Laboratory Service (NHLS)’ electronic laboratory data warehouse, known as the Corporate Data Warehouse (CDW).

We used routinely collected laboratory information to generate surveillance estimates to monitor syphilis trends among women of reproductive age. We extracted over 8.4 million syphilis tests for the period 2003-2012 from the NHLS CDW, a data repository for all public sector laboratory measurements in South Africa. Analysis was limited to females of reproductive age, 12-49 years, and the Northern Cape Province, a region with high syphilis burden. The dataset was de-duplicated using probabilistic record linkage techniques. We applied the Chi-square test of trend to determine whether there was a decreasing trend in syphilis seroprevalence from 2003 to 2012. We used Poisson regression to estimate prevalence ratios (PR) of syphilis seroprevalence over time in STATA version 13. A p-value of less than 0.05 was considered statistically significant.

286 024 women were included in the study. Out of 154 women for whom population group (race) was captured, 132 (86%) were black. Overall, syphilis seroprevalence decreased between 2003 (5.7%) and 2012 (1.8%); p-trend=0.001, among all age groups (12-17 years: 4.2%-2.2%; 18-25 years: 5.7%-1.8%; and 26-49 years: 5.9%-1.7%). See Table 1 for details. The observed decreasing trend in syphilis seroprevalence was consistent with findings published from ANSUR from 2003 (8.6%) to 2011 (3.8%). See figure 1 for details. Three out of five districts had significant decreases in syphilis seroprevalence over the period. There were also declines in PR from 2003 to 2012 for the various age groups and districts. For age, 12-17 years: 10% decrease (PR=0.90; 95% CI=0.80-0.92; p<0.001); 18-25 years: 13% decrease (PR=0.87; 95% CI=0.86-0.88; p<0.001); and 26-49 years: 15% decrease (PR=0.85; 95% CI=0.84-0.86; p<0.001); for districts, Frances Baard (18%); John Taolo Gaetsewe (13%); Namakwa (11%); Siyanda (11%); and Pixley Ka Seme (5%).

The findings of our study were consistent with decreasing trends in syphilis seroprevalence from the ANSUR. The public health implication of our study is that evidence-based estimates of the burden of disease at both provincial and national levels can serve as useful tools in surveillance and in informing the planning and allocation of health resources. We recommend that CDW be considered for annual syphilis seroprevalence monitoring given it provides stable prevalence estimates through broader geographical coverage and larger sample size.
Figure 1: Syphilis seroprevalence for NCP for current study (2003-2012) and ANSUR data (2003-2011).

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<td>(5.5)</td>
<td>322</td>
</tr>
</tbody>
</table>

Table 1: Syphilis seroprevalence among females of reproductive age, Northern Case Province: 2003-2012
SAVE THE DATE! Remember Cape Town 2014? Next stop, Hyderabad!!

17th International Congress on Infectious Diseases

HYDERABAD • INDIA
MARCH 2~5, 2016

Organized by the
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