THE FEDERATION OF INFECTIOUS DISEASES SOCIETIES OF SOUTHERN AFRICA

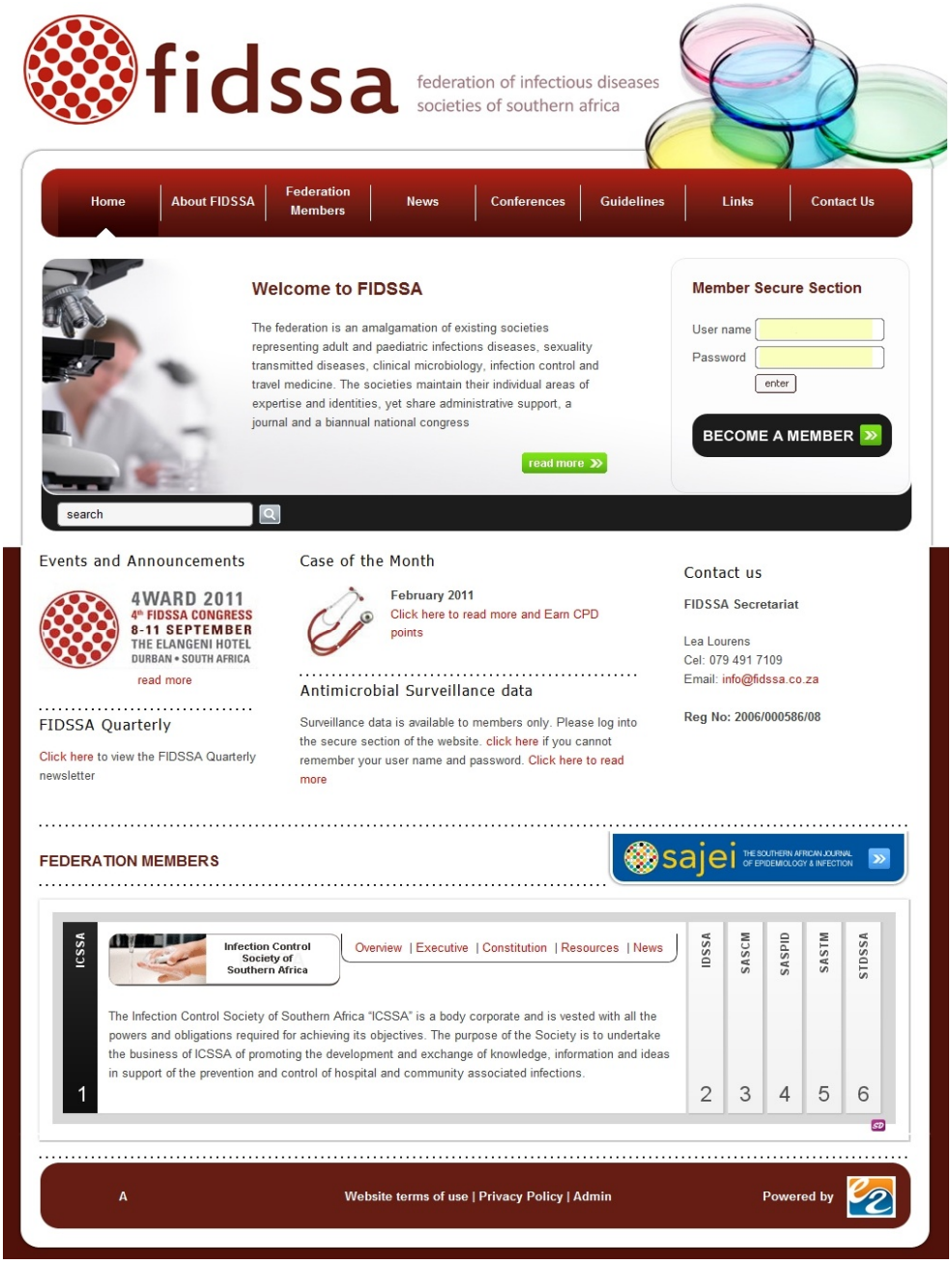
FIDSSA Quarterly

Volume 2 Issue 1 1st March 2011

Special points of interest:

- New look FIDSSA website
- FIDDSA-GlaxoSmithKline research fellowship applications open
- Membership news
- Access to IV artesunate for the treatment of severe falciparum malaria

New look FIDSSA website at www.fidssa.co.za!



We are delighted to announce a new look FIDSSA website: improved formatting, ease of access and more functions. Thanks to our partners at E2 Solutions for re-designing the site!

fidssa federation of infectious diseases societies of southern africa

GlaxoSmithKline

FIDSSA-GlaxoSmithKline Research Fellowships 2011

FIDSSA is delighted to announce a new research fellowship scheme funded by an unconditional educational grant from GlaxoSmithKline.

We will be making 2 awards in 2011, each of R100,000. Funding for laboratory, clinical or public health research projects in the broad field of infectious diseases that FIDSSA represents will be considered. The awards are intended to support new research projects by junior investigators and applicatnts who have not previoulsy received substantial funding (any award > R250,000) will be prioritised.

The following criteria apply to all applicants:

1. Must be a full, paid up 'Ordinary' member of FIDSSA* by the **closing date for applications on 30th June 2011.**
2. Must be a citizen of one of the countries in the southern African region (Botswana, Lesotho, Mozambique, Namibia, South Africa, Swaziland, Zambia and Zimbabwe) and must be undertaking the research project in southern Africa. Applications from southern Africa citizens undertaking periods of research abroad, will not be considered.
3. A fully completed application form downloadable from the FIDSSA website homepage (http://www.fidssa.co.za) or from Lea Lourens at info@fidssa.co.za must be returned to Lea Lourens at info@fidssa.co.za by the closing date (30th June 2011).
4. Applications submitted after the closing date will not be accepted under any circumstances and incomplete applications will be returned to the applicant without review.
5. Each award will be made as a once-off payment in full and the recipients will be announced at the FIDSSA 4WARD conference in Durban 8-11 Sept 2011.
6. Each recipient must undertake to provide a progress report at 6 months, and a final report at 12 months. Any publication arising from work funded by a FIDSSA-GlaxoSmithKline Fellowship, must acknowledge the funding in the manuscript.

Applications open on the 15th March 2011

*Members of SASTM are not eligible to apply unless they are fully paid up members of FIDSSA independent of their SASTM membership.

News from the FIDSSA Office

fidssa federation of infectious diseases societies of southern africa

With 2011 well underway there are still many FIDSSA members that have not renewed their membership for this year. **We would like to remind everyone that you will not reap the benefits if you are not a paid up members for 2011!!** You might have some questions, such as:

What benefits do I get from being a FIDSSA member?

Discounted registration rates for the FIDSSA conference in September
On line CPD points for the monthly case study
Quarterly FIDSSA newsletter
FIDSSA List serve Q&A
Free copy of the SAJEI
And much more!

When do I need to pay my membership fee?

Renewal of membership is **annual**. January – December.
The membership fee for the year will be noted on the website www.fidssa.co.za, along with banking details and a credit card facility.
You do not have to have a FIDSSA number to make payment; use your initials and surname as reference.
Please also remember to send through your proof of payment to the admin office.
Fax: 0866 349 839 or e-mail: info@fidssa.co.za. This must be accompanied by some contact detail such as telephone numbers and e-mail addresses, as some members are not on the database anymore and we can't contact to confirm their membership.
When you have made payment, you will receive a confirmation e-mail and new login details for the website within 2 working days. If not please contact the office.
When visiting the website, please take some time to update you details. Please also notify the office of any changes, especially your e-mail address, mobile number and postal address.

How do I know if my membership is up to date?

If you haven't paid your membership since October 2010 you are now due for renewal.

If I have paid my membership, and still don't have access to the website's restricted area, what do I do?

Please resend your proof of payment to the office and we will correct your details.

We would like to thank everyone that has already paid. We hope that you enjoy being a FIDSSA member!
If you have any queries regarding membership or have any comments on how we can approve on our service, please do not hesitate to contact us!

Lea Lourens. FIDSSA administration

Release of Insects carrying a Dominent Lethal gene (RIDL) – Ecological Engineering

SASTM South African Society of Travel Medicine

RIDL is a more sophisticated version of a pest management technique that's been around since the 1950's called SIT [Sterile Insect Technique]. The idea is to create mosquitoes that have two copies of a dominant suicide gene that causes them to die at a specific life stage unless they get a special chemical. A British Biotech Company, Oxitec has modified male Aedes aegypti mosquitoes that need tetracycline to turn off their suicide genes.

These genetically modified mosquito designed to curb the insect's fertility have been released in south-east Asia as part of an ambitious attempt to combat dengue fever that affects up to 100 million people worldwide. In a remote province of Eastern Malaysia these mosquitoes were released into the wild in a two week experiment aiming to see if wild mosquitoes that infect humans with Dengue might eventually be suppressed or eradicated. The mutant male factory mosquitoes mate with the female wild mosquitoes so the next generation have one copy of the dominant suicide gene but no access to tetracycline. In practical terms this means the pupae can't mature and die.

The only previous release of these mutant mosquitoes was in the British ruled Cayman Islands, The Cayman project, involving the release of 6 MILLION modified mosquitoes which was successful in reducing the local mosquito population by 80%. If it works for Dengue, then it might work for other mosquito born illnesses such as malaria.

Opponents of the Malaysian release raised a host of scientific worries. One concrete fear raised by GeneWatch is that RIDL might eventually be used to successfully suppress *Aedes aegypti*, which spreads Dengue, thereby opening up a niche that might be filled with a non-targeted mosquito like *Aedes albopictus*, which also lives in Eastern Malaysia and also spreads Dengue. Another, more immediate risk raised in GeneWatch's comments is that about 3% of the released mosquitoes are accidentally female and about 3% of the wild suicidal generation don't actually die. If the suicide genes persist in the wild, the local population might evolve resistance that makes future management more difficult. Countering this last point, the Malaysian government asserts that all the experimental mosquitoes were killed by spraying at the end of the experiment.

The big hope in all this is that Oxitec's approach to mosquito control could be hugely important for diseases in the developing world, and RIDL is the logical cautious next step in this area because it isn't intended to persist in the environment. If it works correctly, each application is a one time shot. If humanity is going to practice injecting new genes into the natural world, RIDL is the sort of thing to practice with.

Pete Vincent

HPV Vaccine prospects for South Africa

From the Sexually Transmitted Infections Reference Centre (STIRC), National Institute for Communicable Diseases (NICD), National Health Laboratory Services, Johannesburg.

Human papillomaviruses (HPVs) are one of the most important causes of sexually transmitted infections in both men and women worldwide because of their association with anogenital cancers. Apart from cervical cancer, HPV is also the most common causative agent of genital warts and other squamous intraepithelial lesions (SIL). At least 16 high-risk (oncogenic) HPV types, such as HPV 16, 18, 31 and 45, are implicated in cervical cancer. Low-risk HPV subtypes, such as 6 and 11, are responsible for more than 90% of genital warts and 10% of low grade cervical abnormalities.

There are currently two non-infectious recombinant prophylactic HPV vaccine options Both vaccines are prepared from highly purified virus-like particles. The first HPV vaccine, Gardasil® (Merck & Co.), is a quadrivalent vaccine which targets HPV types 6, 11, 16 and 18.

A second HPV vaccine Cervarix™ (GSK), was approved and registered with the MCC in 2008. This bivalent vaccine was developed to prevent infection and lesions from HPV types 16 and 18. Both Gardasil® and Cervarix™ protect against the two types responsible for over 70% of cervical cancer cases and approximately 50% of high-grade cervical abnormalities. Gardasil® has the additional benefit of providing protection against genital warts.

Both vaccines are very safe, well-tolerated and effective and have demonstrated efficacy of more than 80% against persistent HPV types 16 and 18 infection after 3 doses of HPV vaccine. Harper *et al*. (2006) reported that antibody levels dropped by about one log between the peak after the third dose and 18 months after vaccination and then leveled off conferring adequate antibody levels for at least 5 years post vaccination. The vaccine efficacy for precancerous lesions caused by HPV types 16 and 18 was 98% for Gardasil® and 90% for Cervarix. The Gardasil® vaccine also demonstrated 97% efficacy against vulvar and vaginal intraepithelial neoplasias caused by HPV types 16 and 18 and 96% protection against genital warts. No data are available on the cross-protective effect of the Gardasil® vaccine although some cross-protection was observed for the Cervarix. The efficacy and safety of HPV vaccination in immunocompromised individuals and the safety of vaccination in pregnant women are not yet established.

HPV vaccination should be offered to females up to the age of 26 during the vaccine roll-out period. Current recommendations suggest that vaccination must be determined for each individual population but ideally girls should be routinely vaccinated before the age of sexual debut. The suggested age for HPV vaccination is 11-12 years but this could be as low as 9-10 years. Older women will only benefit from vaccination if they want to prevent new HPV infections. The efficacy of the vaccines in preventing anogenital cancers among men has not yet been established and vaccination in this population is not currently recommended.

Dr Etienne Muller

Improving our response to MRSA infections

Data from 9 academic hospitals in 2004 showed that of a total of 1,841 *Staphylococcus aureus* isolates cultured from invasive infections, 52% were methicillin-resistant. Repeat surveillance in 2007 at 7 NLHS laboratories throughout South Africa reported rates of cloxacillin and clindamycin resistance ranging from 30% to 69%, and 5% to 48%, respectively. Proportions of isolates attributable to childhood infections were not reported in these surveys. However, clinical experience indicates that MRSA is an important pathogen in paediatric practice in South Africa.

Recent anecdotal cases of recurrent MRSA infection and / or vancomycin treatment failure at Red Cross War Memorial Children's Hospital suggested that we should pay closer attention to the management of these infections at our own hospital. Consensus recommendations for treating skin, soft tissue and invasive MRSA infections in children and adults were published in a February 2011 edition of Clinical Infectious Diseases [CID 2011;52(3):285-292 & CID 2011;52(3):e18-e55].

These papers provide useful practical guidelines for optimising treatment. I would like to mention several points applicable to paediatric practice:

- For community-acquired skin and soft-tissue infections (SSTIs) outpatient antibiotic options include clindamycin and possibly trimethoprim-sulphamethoxazole.
- For children with community-acquired infection who require hospitalisation for deep-seated skin / soft-tissue infections vancomycin is the recommended antimicrobial. Clindamycin, 10-13 mg/kg/dose, 6-8 hourly, intravenously may be considered for empirical therapy in settings where clindamycin resistance rates are low.
- For recurrent MRSA SSTIs, nasal and topical body decolonisation should be considered. Details are included in the manuscripts.
- The recommended dose and frequency of vancomycin for all MRSA infections in children is 15 mg/kg/dose, 6-hourly, intravenously.
- The addition of rifamipicin and gentimicin to vancomycin is not recommended for bacteraemia or native valve infective endocarditis.
- For infective endocarditis involving a prosthetic valve the addition of rifampicin and gentimicin to vancomycin therapy should be considered.
- For MRSA pneumonia vancomycin is recommended. In stable patients without bacteraemia or intravascular infection clindamycin may be considered if resistance rates are low.
- For septic arthritis and osteomyelitis intravenous vancomycin is recommended. Empirical clindamycin may be used if the rate of resistance is low. Minimum duration of antibiotics for septic arthritis is 3-4 weeks and 4-6 weeks for osteomyelitis.
- Recommendations for drug monitoring, treatment of persistent bacteraemia and vancomycin treatment failures, and the treatment of MRSA isolates with a vancomycin MIC > 2 μg/ml are included.
- Dosing recommendations for alternative antibiotics such as daptomycin and linezolid are provided.
- The preferred antimicrobial duration for each infection type is included.
- Treatment should be complemented by optimal infection control practice.

Vancomycin remains the most important antimicrobial for treating MRSA infections in children in South Africa. Compared to b-lactam antibiotics, vancomycin kills staphyloccoci more slowly and is inferior in methicillin-sensitive *Staphylococcus aureas* infections. To lower the risk of vancomycin resistance developing, rigorous attention should be given to dosing instructions. Monte Carlo simulation recently showed that at if dosed at 10 mg/kg/dose 6-hourly only 58-66% of children achieved the target AUC_{0-24}/MIC ratio of > 400 compared to 88-98% of children who were given 15 mg/kg/dose 6-hourly, the dose recommended in the new guidelines. Furthermore, the duration of antibiotic administration should be optimised, and routine trough serum concentrations considered. As infectious diseases sub-specialists we have a responsibility to improve antibiotic stewardship in our institutions. These guidelines should certainly assist that process.

Brian Eley

Red Cross War Memorial Children's Hospital and the University of Cape Town

Doripenem (Doribax®): The new Carbapenem on the block

Doripenem is the latest b-lactam carbapenem to be released, and like other b-lactams, exerts its bactericidal activity by inhibition of bacterial cell wall biosynthesis.

So what is different about doripenem?

Doripenem combines the intrinsic activity of meropenem against gram-negative bacteria (including extended-spectrum B-lactamase [ESBL]-producing strains) with the intrinsic activity of imipenem against gram-positive pathogens and anaerobes.

Doripenem shows potent *in vitro* activity against resistant gram-negative bacteria, such as *Pseudomonas aeruginosa,* with MIC90 values that are 2–4 times lower than the corresponding MIC90 values for meropenem and imipenem.

It is indicated for the treatment of the following infections in adults:
1. Nosocomial pneumonia (including ventilator–associated pneumonia)
2. Complicated intra-abdominal infections
3. Complicated urinary tract infections

Prescribing information

Doripenem is administered by intravenous infusion over a period of 1-4 hours. Extending the infusion time to 4 hours maximizes the time that the plasma concentration of doripenem exceeds the minimum inhibitory concentration (%T>MIC), which correlates with efficacy in PK/PD studies.

The recommended dosage and administration by infection is shown in the following table:

Infection	Dosage	Frequency	Infusion
Nosocomial pneumonia including ventilator–	500 mg	every 8 hours	1 or 4 hours*
Complicated intra-abdominal infection	500 mg	every 8 hours	1 hour
Complicated UTI, including pyelonephritis	500 mg	every 8 hours	1 hour
*Based mainly on PK/PD considerations, a dose of 1g 8hrly as 4-hour infusion may be more suitable for infection with less susceptible pathogens such as *Pseudomomas aeruginosa.* This dosing regimen should also be considered in particularly severe infections.			

Treatment duration is generally 5-14 days, guided by severity & site of infection, and clinical response.

Low protein binding facilitates good penetration of doripenem into tissues and body fluids.

Doripenem undergoes little to no Cytochrome P450 (CYP450) mediated metabolism. Therefore, no CYP450-related drug interactions are to be expected.

No dosage adjustments are necessary in patients with impaired hepatic function, mild renal insufficiency or the elderly. Dosage adjustments are required in patients with moderate to severe renal impairment.

Doripenem is not recommended for use in children <18yrs and pregnant women due to insufficient data.

The most common adverse reactions are headache, rashes, nausea and diarrhoea.

Mechanisms of resistance
Bacterial resistance mechanisms that affect doripenem include active substance inactivation by carbapenem-hydrolysing enzymes, mutant or acquired penicillin binding proteins (PBP's), decreased outer membrane permeability and active efflux. Doripenem is stable to hydrolysis by most beta-lactamases, including penicillinases and cephalosporinases produced by gram-positive and gram-negative bacteria, with the exception of relatively rare carbapenem hydrolysing beta-lactamases. Species resistant to other carbapenems do generally express co-resistance to doripenem. The administration of higher dosages by prolonged infusions may be less likely to select for resistant mutants in infections caused by less-susceptible pathogens such as *Pseudomonas aeruginosa*. Methicillin-resistant staphylococci should always be considered as resistant to doripenem.

References: Sahm. CID 2009:49 (Suppl 1) ; Chastre et al. Crit Care Med 2008; 36:1089-1096
http://www.medscape.com/viewarticle/733351 Doribaxpackage insert, Janssen Phamaceuticals

Infection Control News

The Best Care…Always (BCA) Campaign is expanding further into other provinces, and a workshop was held in the Western Cape on 23 and 24 February (unfortunately no feedback at the time of writing this newsletter, but we will feed back in the next edition). The BCA task team has also summarised the definitions of surgical site infections, ventilator associated pneumonia, catheter related UTI and central line associated blood stream infections. These new, (hopefully) easier to read definitions will have been posted on the BCA website by the time you read this, and as always, we encourage you to visit the website regularly to get updates (www.bestcare.org.za).

I hope as many people as possible are planning to come to the FIDSSA congress from 8-11 September. We would like to see a large contingent of IPCs at the sessions and of course at the AGM. Dr Theresa Horan from the CDC will be a guest speaker, as will Dr Geoff Abbott from the CSIR. Dr Horan's expertise is in surveillance of nosocomial infections, in particular how to define and measure these infections, while Dr Abbott has significant expertise in hospital design, especially as it affects TB infection control. Of course there will be a range of local speakers, and I would strongly urge anyone who wants to present their own research to submit an abstract. We (the committee) are always available to offer advice and support if necessary.

The Infection Prevention and Control African Network (IPCAN) conference will be held in Namibia from 31 October to 3 November; visit the congress website for more details (http://www.ipcan.co.za). The Western Cape chapter is hosting an injection safety workshop on the 6th April at Tygerberg Hospital. Please contact Yolanda van Zyl (yvanzyl@pgwc.gov.za) for more details or to RSVP.

Finally, we unfortunately have to say farewell to Shamane Gavripersad, who was co-ordinating the KZN chapter of ICSSA and representing ICSSA on the local organizing committee. Unfortunately Shamane has become a Theatre Manager (operating theatre, not acting…), which is great for her career but unfortunately means we lose another enthusiastic IPC. This does unfortunately once again illustrate the ongoing difficulty of retaining IPCs (in state and private sector), with the lack of well defined career paths in Infection Control. Yolanda Janse van Rensburg has volunteered to take over co-ordinating a Pietermaritzburg chapter, and we wish her much success. If anyone in KZN would like to get involved, please contact Yolanda (yolanda.jansevanrensburg@mediclinic.co.za) or myself (andrew.whitelaw@uct.ac.za).

And on that note, Cheers for now.

Access to artesunate; a giant step forward

Intravenous artesunate is recommended by the World Health Organisation (WHO) as the treatment of choice for severe falciparum malaria in adults. A significant mortality benefit (34.7% relative reductions compared to intravenous quinine) has been shown for adult patients with severe malaria[1] and for children (22.5% relative reduction)[2]. For every 11 to 20 adult patients (or 41 children) with severe malaria treated with iv artesunate instead of iv quinine, one life is saved. Intravenous artesunate kills parasites more rapidly, has a safer side-effect profile and is easier to administer.

Since June 2007, efforts have been underway to facilitate access to iv artesunate in South Africa, starting with motivation by the Malaria Advisory Group to the Department of Health. In June 2009, the Medicines Control Council approved the use of iv artesunate for the treatment of adults with severe malaria and in October of the same year. This drug was procured from Guilin Pharmaceuticals, China, and independently quality assured. Since December 2009, 22 sentinel hospitals, selected for their treating most of the severe malaria cases in South Africa were chosen and started treating patients with iv artesunate under an expanded access Section 21 programme. On-site training was provided and stringent adherence to the MCC Section 21 reporting requirements was ensured. In February 2011, the Medicines Control Council approved continuation of this access programme and its extension to include children with severe malaria.

To expand the access of iv artesunate to futher hospitals in South Africa, the following responsibilities must be undertaken.

A) A named responsible doctor at the hospital must:

1. Provide support to ensure optimal case management of all patients with severe malaria
2. Ensure that informed consent is obtained from the patient/guardian/next of kin or medical superintendent for each patient treated with iv artesunate
3. Notify the iv artesunate access programme secretariat of each patient treated with iv artesunate within 1 working day of treatment being stated
4. Complete a Case Management Record for each patient treated

B) A responsible pharmacist must ensure secure storage of the drug under appropriate condtions, arrange after-hours access to ensure prompt treatment and complete iv artesunate drug accountability documents.

For further information about accessing iv artesunate at your hospital, please contact Dr Elsime Visser-Kift (Elsime.Visser-Kift@uct.ac.za) in the department of Clinical Pharmacology at the University of Cape Town.

1, SEQUAMAT group. Intravenous artesunate versus quinine for treatment of severe malaria: a randomized trial. Lancet 2005; 366: 717-25.

2, AQUAMAT group. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. Lancet 2010; 376: 1647-57.