Link

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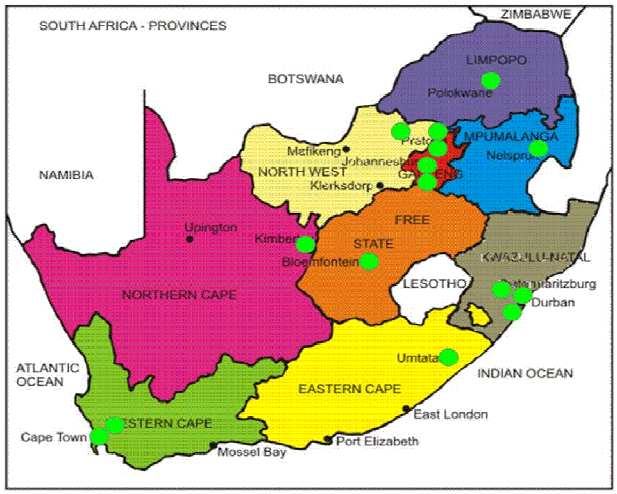

Second Quarter

GERMS-SA: The year thus far

We've reached the halfway mark and we're pushing through with as much energy as always. We've had to say goodbye to Grey's, Victoria and Rustenburg from the enhanced surveillance platform but we've welcomed Klerksdorp/Tshepong.

TB surveillance continues to be rolled-out across the country and to date we have sites in North West, Gauteng, Mpumalanga, Limpopo, Northern Cape and Eastern Cape.

The second half of the year holds much excitement such as we will be hosting our second Surveillance Officer meeting for 2013, the annual Principal Investigators meeting 2013 and the long awaited launch of the cellular phone-based data collection for GERMS-SA. Watch out, change is coming through.

In this edition of the LINK you can find; a very insightful look at amphotericin B-related toxicities (pg 2), feedback from the inaugural mid-year programme review meeting (pg 4) and the 6th SA-AIDS conference recently held in Durban (pg 5), the enhanced surveillance site operation report summary (pg 6), site visit reports (pg 8) and our customary reminder (pg 10). Happy reading!

[Nevashan Govender—GERMS-SA]

Preventing, monitoring and managing amphotericin B-related toxicities when treating cryptococcal meningitis - Susan Meiring

Over the past 10 years, despite an increase in amphotericin B use as induction therapy for cryptococcal meningitis (CM), in-hospital mortality rates for CM remain unchanged at approximately 30%. Amphotericin B, in combination with flucytosine or fluconazole, is the recommended first line therapy for CM, however if used incorrectly it has the potential to cause serious toxicities including nephrotoxicity and hypokalaemia. In response to this the WHO Rapid Advice on Cryptococcal Management, published in December 2011, included a minimum package for the prevention, monitoring and management of amphotericin B toxicities (Box 1).

Our study aimed to compare the differences in clinician awareness and adherence to these guidelines at academic versus non-academic hospitals in South Africa. We used our GERMS-SA surveillance network to interview clinicians regarding CM treatment and prevention/monitoring practices when using amphotericin B. The GERMS-SA surveillance officers also collected data on the treatment and management of patients with CM admitted to these hospitals between October 2012 and February 2013.

Forty-two clinicians were interviewed, 21 from academic and 21 from non-academic sites. There were no significant differences found in the responses between clinicians from the different hospital settings. Sixty-eight percent followed some guideline of CM management, however only 25% of these were aware of the WHO Rapid Advice Guidelines. 95% said that they used amphotericin B as first line therapy and 90% were aware of the complications of amphotericin B use. 78% of clinicians said that they gave pre-emptive hydration and electrolyte supplementation to patients whilst on amphotericin B, while 90% said that they checked the creatinine and potassium levels at baseline and during amphotericin B therapy.

We were able to review the medical records of 659/752 patients presenting to 26 GERMS-SA enhanced surveillance sites (56% were from academic and 44% from non-academic sites). Overall 81% of patients received amphotericin B therapy. Amphotericin B toxicity prevention parameters (baseline electrolyte testing, pre-emptive hydration and electrolyte supplementation) were implemented poorly (less than 60%) at both hospital settings, however electrolyte supplementation was significantly more likely to occur at academic than non-academic sites.

Monitoring for amphotericin B toxicities (fluid input/output, biweekly serum potassium and creatinine, weekly haemoglobin) was suboptimal (less than 50%) for all parameters measured, except fluid input/output measurements (87%). Academic sites were significantly better at monitoring for all the parameters measured than non-academic sites.

This study highlights the lack of adherence at both academic and non-academic hospitals to already published guidelines aiming to prevent, monitor and manage amphotericin B toxicities. The HIV clinicians Society recently published updated guidelines on the management of CM, and these too include a recommendation for prevention and monitoring for amphotericin B toxicities. The challenge now is to make clinicians aware of the importance of adhering to guidelines especially when treating patients with potentially toxic antifungal agents such as amphotericin B.

Box 1: Minimum package for amphotericin B toxicity prevention, monitoring and management

Pre-emptive hydration and electrolyte supplementation[17]

- Adults and Adolescents:
  One litre of normal saline solution with one ampoule (20 mmol) of KCL over 2-4 hours before each controlled infusion of amphotericin B (with one litre of 5% dextrose) and one to two 8mEq KCL tablets orally twice daily. An additional one 8mEq KCL tablet twice daily may be added during the second week. If available, magnesium supplementation should also be provided (two 250mg tablets of magnesium trisilicate twice daily).
- Children less than 5 years:
  Up to one litre of normal saline solution with one ampoule (20 mmol) of KCL at 10-15 ml/kg over 2-4 hours before each controlled infusion of amphotericin B. If saline is unavailable, then other intravenous rehydration solutions that contain potassium can be used eg. Darrow's or Ringer's Lactate solutions.
- Potassium replacement should not be given patients with pre-existing renal impairment or hyperkalaemia.
- A test dose for amphotericin B is not recommended

Monitoring

- Serum potassium and creatinine (baseline and twice weekly), especially in the second week of amphotericin B administration.
- Haemoglobin (baseline and weekly)
- Careful attention to fluid monitoring of intake and output, and daily weight

Management

- If significant hypokalaemia (K <3.3mmol/l), increase potassium supplementation to two KCL ampoules (40 mmol), or one or two 8mEq KCL tablets three times daily. Monitor potassium daily.
- If hypokalaemia remains uncorrected, double magnesium oral supplementation
- If creatinine increases by ≥2 fold from baseline value, either temporary omission of an amphotericin B dose, or increase pre-hydration to one litre 8 hourly. Once improved, restart at 0.7 mg/kg/day and consider alternate day amphotericin B. If creatinine remains elevated, discontinue amphotericin and continue with fluconazole at 1200mg/day. Monitor creatinine daily.

South African Cryptococcal Screening Programme - Verushka Chetty

The Birchwood Conference Centre was a hub of activity during 22-23 May 2013. The occasion? The inaugural mid-year programme review meeting for the South African Cryptococcal Screening Programme. Over 120 Delegates descended from all parts of South Africa and abroad and included provincial and national counterparts, colleagues from Mycotic Diseases Branch (CDC-Atlanta), PEPFAR implementing partners, as well as representatives from African countries such as Mozambique, Namibia and Botswana.

Dr Thobile Mbengashe reiterated the commitment of the South African government to reducing disability and deaths associated with serious OIs.

Conference participants eagerly watching the CrAg test as demonstrated by Thokozile Zulu .

What a team! Thank you to everyone who participated to make this meeting a success.

6th SA-AIDS Conference, Durban, 18-21 June 2013 - Susan Meiring

Durban, in winter, is definitely the place to be…especially if you wished to attend the SA-AIDS conference held at the Durban International Convention Centre from 18 to 21 June 2013.

The warm winter days reflected the vibrancy of the conference delegates as they rushed between the packed sessions celebrating the many successes achieved thus far in the fight against HIV/AIDS.

I was there to present at a skills building workshop focusing on the new cryptococcal meningitis treatment guidelines which have been recently published by the South African HIV Clinicians Society. Dr Nelesh Govender, former head of GERMS-SA and currently heading up the Mycology Reference Laboratory at the NICD, was the convenor of the session and was integral in the formulation of these guidelines (and the former guidelines) on the management of cryptococcal disease. It was encouraging to know that our GERMS-SA surveillance data on patients with cryptococcosis played an important role in the discussions that brought about these guidelines.

The highlight of the conference, for me, was the release of the preliminary results of the Health Science Research Council (HSRC) 2012 National HIV Household Survey, by Prof Olive Shisana. Key findings from this survey reported a national HIV-prevalence of 12.3%, with over 2 million HIV-infected persons currently on antiretroviral therapy. HIV-incidence was not yet available, but these findings suggest that the slight rise in HIV-prevalence may be due to less rates of death amongst those who are HIV-infected.

One of the greatest successes has been seen with the revamp on the Prevention of Mother To Child Transmission programme which has resulted in a decline in HIV-prevalence amongst children (2-14 years of age) from 9.6% in 2002 to 2.9% in 2012. This survey also showed a drop in condom use and an increase in multiple sex partners across all age bands since 2008, highlighting that sexual behavioural practices still need to be addressed in order to prevent new HIV infections.

All in all the conference was a great opportunity for researchers to showcase how they are aiming to conquer the virus as we all take up the challenge of "Getting to Zero: zero new HIV infections, zero discrimination and zero AIDS-related deaths".

Enhanced Surveillance Site Operation R

JANUARY TO MARCH 2012						
Lab confirmed cases*	**# CRFs com-pleted**	**% CRFs**	**# Interview**	**% Interview**	**Province**	**ES Si**
42	33	79	18	55	EC	NMA
36	27	75	26	96	FS	Universitas/
167	104	62	64	62	GA	CHBH
92	71	77	55	77	GA	CMJAH
52	30	58	26	87	GA	DGM
35	28	80	28	100	GA	SBAH
					GA	Rahima Mo
39	32	82	24	75	KZ	Adding
80	70	88	52	74	KZ	Greys/ Ed
19	5	26	3	60	KZ	KEH
59	34	58	32	94	KZ	RK Kh
22	9	41	9	100	LP	Polokwane/ M
54	46	85	38	83	MP	Rob/ Tho
25	21	84	16	76	NC	Kimbe
58	47	81	26	55	WC	GSH/ RXH/
30	18	60	7	39	WC	Tygerbe
810	**575**	**71**	**424**	**74**		**TOTAL**

* Includes all IPD cases

** Unknown data for the interview question: Did the patient receive TB treatment in the past 3 months?

Target met	Target not met

Targets: ≥90% for CRFs completed; ≥60% for CRFs completed on interview

> Compared to data from Q1 ESSOR 2012, the total number of cases for 2013 increased and both the overall % of completed CRFs and %

> The main increase in laboratory-confirmed cases was due to inclusion of *Staphylococcus aureus (sites marked $) and Candidaemia (site* surveillance into these reports.

> Only Greys/Northdale/Edendale reached the target of 90% for completed CRFs - this is disappointing for the other sites.

> 15/16 sites reached the target of 60% for completed CRFs on interview; this target was far exceeded at most sites - excellent work!

> CHBH, DGM, Greys/Edendale/Northdale, KEH, RK Khan and Polokwane improved their % of CRFs completed

> NMAH, CHBH, CMJAH, DGM, Greys, KEH, Kimberley, GSH/RXH and Tygerberg improved their % of interviews

> DGM, SBAH, Greys/Edendale, RK Khan, Polokwane and Tygerberg achieved between 90% and 100% on interview - excellent!!

> Sites with less than 65% of completed CRFs need to urgently improve their rate of completion of CRF

Report Summary - First quarter, 2013

	JANUARY TO MARCH 2013					
Site	Lab confirmed cases*	# CRFs completed	% CRFs	# Interview	% Interview	# Unknown data**
AC	56	41	73	24	59	1
Pelonomi	27	16	59	14	88	0
H $	241	163	68	126	77	5
H $,^^	232	164	71	133	81	12
M	35	27	77	27	100	0
H $,^^	88	21	24	20	95	0
oosa $,^^	82	58	71	58	100	0
gton	33	22	67	14	64	0
dendale	114	105	92	102	97	0
H	36	12	33	10	83	0
han	44	36	82	34	94	0
Mankweng	22	14	64	13	93	1
emba	60	39	65	31	79	1
erley	20	13	65	11	85	0
Victoria $	114	89	78	55	62	0
erg $	45	26	58	24	92	1
	1249	**846**	**68**	**696**	**82**	**21**

% of interviews increased - Well done!

es marked ^^) enhanced

GERMS-SA on the move: Site visits

Natalspruit Hospital - 4th June 2013

The people in white coats will be coming to take me away if I stay in this job much longer: Claire von Mollendorf (extreme left), Mmakgomo Rakhudu (front row, fourth from the left), Sarona Lengana (back row, third from the right), and the Natalspruit surveillance officer Nokubonga Ndaba (extreme right) with NHLS laboratory staff at the Natalspruit hospital.

Natalspruit hospital became one of our newest sites for the IPD case-control study and for enhanced cryptococcal surveillance in March 2013. A site visit was conducted in June 2013 with the objectives of introducing GERMS-SA and the IPD case-control study to the clinical managers, and to explain the processes the surveillance officer follows in identifying cases. There were very good discussions and action plans formulated from this visit that should address issues surrounding case identification and isolate submission.

Klerksdorp/Tshepong Hospital - 4th July 2013

We do not travel light (from left to right): Jabu Mabuyakhulu, Claire von Mollendorf, Sonwabo Lindani and Linda Erasmus are armed with everything but the kitchen sink for their site visit.

It is not all fun and games: Sonwabo Lindani (extreme right) puts a humorous twist on some serious training of surveillance staff at the Klerksdorp/Tshepong hospital.

It was with much sadness that we said to goodbye to Rustenburg/Job Shimankana Tabane hospital as our enhanced surveillance site in the North West province. However, it was with great excitement and vigour that we welcomed Klerksdorp/Tshepong hospital onto the enhanced platform along with new surveillance officer Joyce Tsotsotso as of July 2013.

Dr Variava, the site coordinator at Klerksdorp/Tshepong, was very excited about being part of the GERMS-SA surveillance network and has aspirations of using the platform for additional surveillance related projects. This excitement is echoed by the GERMS-SA coordinators as Klerksdorp/Tshepong is our first fully integrated GERMS-SA/SARI site. This means that all GERMS-SA/SARI work will be shared amongst the team that will be overseen onsite by Bekiwe Ncwana.

We hope that this site will be a template for things to come for GERMS-SA.

General information for surveillance laboratories

Surveillance organisms and sites

Please submit the following bacterial and fungal pathogens to the National Institute for Communicable Diseases (NICD) on Dorset Transport Media with a completed sterile site isolate form or stool isolate form or DISALab/ TrakCare Lab form.

Pathogen	Specimen	Lab tests	NICD Unit
Streptococcus pneumoniae *Haemophilus* spp. *Neisseria meningitidis*	All normally sterile site specimens, e.g. CSF, blood, pleural fluid, peritoneal fluid, pericardial fluid, joint fluid, tissue, etc.	Culture positive **OR** Consistent Gram stain plus latex antigen test positive	CRDM
Salmonella spp. (including *Salmonella* Typhi) *Shigella* spp.	Any specimen	Culture positive	CED
Diarrhoeagenic *E. coli* *Vibrio cholerae*	Gastrointestinal specimens, e.g. stools, rectal swabs, etc.	Culture positive	CED
Cryptococcus spp.	Any specimen	Culture positive **OR** Latex positive **OR** India ink positive	COTHI (MRL)
† *Candida* spp.	Blood culture only	Culture positive	COTHI (MRL)
**Staphylococcus aureus*	Blood cultures only	Culture positive	COTHI (AMRRL)

† Chris Hani Baragwanath, Charlotte Maxeke Johannesburg Academic, Helen Joseph, Groote Schuur, Steve Biko Pretoria Academic, Tygerberg

*Charlotte Maxeke Johannesburg Academic, Steve Biko Pretoria Academic, Helen Joseph/ Rahima Moosa Mother and Child Hospital

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