“OUT OF AFRICA”

Adriano G Duse
MT, MBCh (Rand), DTM&H, MMed (Micro), FCPath (SA)
Chief Specialist, Professor & Academic Head
Department of Clinical Micro- and Inf. Diseases
NHLS and Wits School of Pathology, South Africa

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com

Objectives Of Presentation:

- Background information to South African hospitals
- Organisms that are “Out of Africa”
- MDR within the South African context with nosocomial / transnational / transcontinental spread
- Coping with limited resources – redefining the gold standard
- The good, the bad, and the ugly
- The way ahead for South Africa: a land of contrasts
- Conclusions

“Ex Africa semper aliquid nova”

Pliny the Elder (23-79 AD)

“Ex Africa Semper Aliquid Nova”

- Index case:
  - 46y old anaesthetic assistant, private clinic in Johannesburg
  - 2/11/96: ill with fever
  - 5/11/96: severe headache
  - 6/11 to 13/11: admitted, leukopaenia, thrombocytopenia, deranged LFTs, deteriorating renal function - dialysis (13/11)
  - 14/11: presumptive laboratory diagnosis of Ebola virus; definitively confirmed 15/11
  - 16/11 to 22/11: T/F to JH ICU, critical condition, haemorrhaging, secondary nosocomial bacterial and fungal infections, large intracranial haemorrhage (22/11)
  - 24/11/96: demised

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com
“Ex Africa Semper Aliquid Nova”

- Primary case/source:
  - Very ill 40 y old doctor transported by air from Libreville, Gabon; admitted to private clinic on 27/10/1996
  - 29/10/1996: Index case (anaesthetic assistant) exposed to large amount of his blood during CVC insertion and subsequent cleaning-up process
  - Unusual presentation - misdiagnosed as suffering from a polymyositis-overlap syndrome - given hydrocortisone - prompt improvement - discharged 11/11/1996
  - 16/11/1996 traced to a convalescence home. Ebola titres >1/512 confirmed he was primary case

- Nosocomial implications: critical retrospective review of South African VHF infection control practices

South African Public Health System, 2001
(source: M Hensher EU Consultant in Health Economics, DOH, SA)

<table>
<thead>
<tr>
<th>Hospital type</th>
<th>#beds</th>
<th>Beds/1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tertiary</td>
<td>23 273</td>
<td>0.61</td>
</tr>
<tr>
<td>Regional</td>
<td>19 244</td>
<td>0.51</td>
</tr>
<tr>
<td>District</td>
<td>36 622</td>
<td>0.97</td>
</tr>
<tr>
<td>CH centres</td>
<td>456</td>
<td>0.01</td>
</tr>
<tr>
<td>Specialised hospitals</td>
<td>20 939</td>
<td>0.55</td>
</tr>
<tr>
<td>Total</td>
<td>100 535</td>
<td>2.65</td>
</tr>
</tbody>
</table>

South African Public Health System, 2001
(source: M Hensher EU Consultant in Health Economics, DOH, SA)

<table>
<thead>
<tr>
<th>Deaths &amp; discharges= Admissions</th>
<th># Admissions</th>
<th>Admission rate/1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tertiary</td>
<td>766 928</td>
<td>20.2</td>
</tr>
<tr>
<td>Regional</td>
<td>878 262</td>
<td>23.1</td>
</tr>
<tr>
<td>District</td>
<td>1 429 667</td>
<td>37.7</td>
</tr>
<tr>
<td>CH centres</td>
<td>22 723</td>
<td>0.6</td>
</tr>
<tr>
<td>Specialised hospitals</td>
<td>79 061</td>
<td>2.1</td>
</tr>
<tr>
<td>Total</td>
<td>3 176 640</td>
<td>83.7</td>
</tr>
</tbody>
</table>

1. South African Hospitals:

- Groote Schuur Hospital (as at May, 2002):
  - OPD: 507 037
  - Acute beds: 1302
  - % Bed occupancy: 74.6%
  - Medical Staff: 644
  - Nursing Staff: 1450
  - Total Annual Expenditure: ~ R 662 m
  - In-patients: 40 640 / year

- Johannesburg Hospital (2002/2003 financial year):
  - In-patients: 68 315
  - Beds in use (mostly acute): 1281
  - % Bed occupancy: 92.7% (but in MAW = 317%; LW =149%; TICU = 128%)
  - Av hosp stay: 5.2 d
  - NI rate: 1.8 %
  - Nurse-to-patient ratio: 0.83
    - In ICUs = 1:1
    - In High Care = 1:4
    - ICN = 4 for 1281 beds; also heavily involved in OHS
South African Hospitals:

- CH Bara Hospital (2001/2)
  - 173 acres; GBR 1997!
  - Admissions: ~ 178 000 / year
  - OPD: 497 273
  - Total # beds: 3400 (currently 2600)
  - Bed occupancy: often up to 350%
  - Total annual expenditure: R 767m

- Rob Ferreira Hospital (2001/2)
  - Admissions: 14619 / year
  - Total # beds: 271
  - Nurse-to-patient ratio: 1:12
  - ICU (4 beds): 1:1:2

Organisms First Discovered In Africa Of Nosocomial Importance: Viruses

- Lassa fever
- Marburg, Ebola viruses
- HIV 1 & 2
- Monkeypox virus

2. Organisms that are “Out of Africa”

Examples Of Nosocomial Pathogens First Discovered In Africa, And/Or Spread On The African Continent, And/Or Exported “Out Of Africa”

- Viruses:
  - Lassa fever
  - Marburg, Ebola viruses
  - Measles virus
  - HIV 1 & 2
  - (WNV, RVF, Chikungunya, Wesselsbron viruses)
  - Monkeypox

- Bacteria:
  - South African pneumococcal strains
  - Salmonella Johannesburch
  - Salmonella isangi
  - Shigella dysenteriae type 1
  - African tick-bite fever (Rickettsiae)
  - (M tuberculosis)

- Parasites:
  - African trypanosomiasis
  - (Plasmodium spp)

Organisms First Discovered In Africa Of Nosocomial Importance: Viruses

<table>
<thead>
<tr>
<th>Agent</th>
<th>Properties and Nosocomial Transmission</th>
<th>Prevention / Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lassa virus</td>
<td>Easily inactivated for safe lab tests (heat 56 C/30 mins; B-propiolactone; formalin; UV radiation Disinfection 0.5% phenolic; 10% hypochlorite; peracetic acid</td>
<td>Infection control (isolation; PPE: gloves, gowns, masks; avoid re-use of inadequately sterilised equipment) Ribavirin (Vaccine)</td>
</tr>
</tbody>
</table>

MARBURG – 1967
(Germany & Yugoslavia exposed to imported african Green Monkeys (Cercopithecus aethiops captured in Uganda); South Africa 1975, Zimbabwe (1975, 1982); Kenya (1980, 1987)

Shown to survive in semen of a convalescent patient for up to 83 d after disease onset; also isolated from anterior of eye of a convalescent patient with uveitis 80 days after disease onset

Infection control (isolation; PPE: gloves, gowns, masks; avoid re-use of inadequately sterilised equipment; sharps & waste disposal; handling of the dead)
### Out of Africa

**Professor Adriano Duse, Johannesburg, South Africa**

**A Webber Training Teleclass**

#### 1. EBOLA VIRUS

**Agent**

- EBOLA VIRUS

**Properties And Transmission**

- EV: isolated from patients 61 days after disease onset.
- Finding of abundant viral antigens & particles in the skin of EHF.
- Possible autologous role for contact transmission.
- Contact with body fluids can lead to transmission.

**Prevention / Treatment**

- Infection control (isolation; PPE: gloves, gowns, masks; avoid re-use of inadequately sterilized equipment; sharps & waste disposal; handling of the dead).

#### 2. CCHF VIRUS

**Agent**

- CCHF VIRUS

**Properties and Transmission**

- Viral survival in used syringes in excess of 7 days at 35°C.
- Tropical ambient temperatures (35°C).
- Viral survival in used syringes can last for 7 days.

**Prevention / Treatment**

- Infection control (isolation; PPE: gloves, gowns, masks; avoid re-use of inadequately sterilized equipment; sharps & waste disposal; handling of the dead).

#### Out of Africa: Viruses

<table>
<thead>
<tr>
<th>Agent</th>
<th>Properties And Nosocomial Transmission</th>
<th>Prevention / Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBOLA VIRUS</td>
<td>EV v isolated from patients 61 days after disease onset. Finding of abundant viral antigens &amp; particles in the skin of EHF. Possible autologous role for contact transmission. Contact with body fluids can lead to transmission.</td>
<td>Infection control (isolation; PPE: gloves, gowns, masks; avoid re-use of inadequately sterilized equipment; sharps &amp; waste disposal; handling of the dead).</td>
</tr>
<tr>
<td>HIV 1 &amp; 2</td>
<td>Viability in syringes for up to 4 weeks. Visible HIV-type seen +21.25 h after death. Viability of HIV in post-mortem samples up to 11 days.</td>
<td>Delay autopsy for 24 h to markedly decrease infectivity. Treatment: PEP.</td>
</tr>
</tbody>
</table>
3. MDR within the South African context with nosocomial / transnational / transcontinental spread

MDR Shigellosis: the South African Experience
- Spread of MDR *Shigella dysenteriae* type 1 infection southwards to South Africa (in 1990s) from other parts of Africa (1970s-1980s) - epidemics in Mpumalanga and KZN
- Nosocomial transmission of MDR *Shigella dysenteriae* type 1 in chronic care psychiatric institution in Durban, South Africa
  - 4/10 patients died
  - IC measures halted outbreak

Organisms First Discovered In Africa Of Nosocomial Importance: Bacteria
- *Salmonella Isangi*
  - First described in Stanleyville “Belgian Congo” – 1947
  - 1999-2001: outbreak of ESBL-producing S Isangi in paediatric wards at CHB
  - May 2002: 18 children at Lambano Baby Sanctuary, 1 death
  - Interventions: IC procedure review and implementation, HCW education, ciprofloxacin administration

Wadula et al: Poster, Joint Congress of HIV Clinicians, ID, IC, Travel Medicine, STD Societies and Veterinary and Public Health, 2-6 December 2001
Govender et al: Poster, 23rd ICC, Durban, South Africa, 7-10 June 2003

Organisms First Discovered In Africa Of Nosocomial Importance: Bacteria
- *Salmonella Johannesburg*
  - First isolated in Johannesburg, South Africa – identified by Kauffmann & Henning (1952)
  - SAIMR Annual Report 1966: alarming increase in incidence of S Johannesburg in Black patients from various hospitals
  - Rare serotype; tendency to produce chronic infection; Strain R to commonly used antibiotics (amp, kana, tet, chlor); apparently higher infectivity
  - Introducion in Hong Kong via imported foods; S. Johannesburg isolated from a dog imported from SA under quarantine in 1974 in HK
  - First detected in HK in 1971 (4 cases), 1972 (783), 1973 (1433), and 1974 (1411)
  - Caused hospital outbreak in Hong Kong in 1974 – in a paediatric general hospital (overcrowding, heavy environmental contamination, no apparent faecal carriage in HCWs), 115 cases (1 Aug – 30 Sept 1974) – 24 (20.9%) primary admission for G/E with S Johannesburg; 22 of remaining initially non-infected children acquired it nosocomially (24.2% cross-infection rate)
  - S. Johannesburg was among the 20 most common salmonella serovars among Canadian registered commercial egg producing flocks (Epidemiol Infect 1991;106:259-270)

Anti-microbial Resistance Within The South African Context: *S pneumoniae*
- Successful global spread of Spanish serotype 23F pneumococcal clone (Spain 23F-1) including to South Africa
- Two pneumococcal clones of serogroup 19A identified in South Africa (PIRP South Africa19A-7, and MDR South Africa19A-13)
- Unique PR serotype 6B clone has emerged locally in South Africa (South Africa6B-8)
Pneumococcal Disease: The South African Experience

- Examples of dissemination through migration:
  - Pneumococcal Epidemiology Network (PMEN) - established 1997 under auspices of the International Union of Microbiological Societies

- Nosocomial transmission:

  Effect of Hospitalisation on Carriage of Pneumococci Among 100 South African Children


Nosocomial Acquisition Of Pneumococci In Children

<table>
<thead>
<tr>
<th>Carriage status</th>
<th>Total # of carriers</th>
<th>Distribution of pneumococci among carriers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On admission</td>
<td>53</td>
<td>Pen S 29 (55) PIRP 17 (32) P(H-L)R 7 (13)</td>
</tr>
<tr>
<td>Persistency</td>
<td>28</td>
<td>Pen S 9 (32) PIRP 8 (29) P(H-L)R 11 (39)</td>
</tr>
<tr>
<td>Acquired</td>
<td>17</td>
<td>Pen S 3 (18) PIRP 13 (29) P(H-L)R 20 (44)</td>
</tr>
</tbody>
</table>

Pneumococcal Disease: The South African Experience

  - NI: 15/457 cases

Tuberculosis: The South African Experience

- Community to Hospital
  - Nosocomial transmission
    - patient-to-patient
    - patient-to-HCW
  - Hospital to Community:
    - Intrafamilial spread in 4 families of MDR-TB from patients treated at Sizwe Hospital

Wooff M, 1988, Presented at ID Congress, Sandton, South Africa

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com
Tuberculosis: The South African Experience

- Nosocomial transmission:
  - patient-to-patient:
  - patient-to-HCW:
    Balt E, et al. Nosocomial transmission of TB to HCWs in Mpumalanga. SAMJ

Control Of Nosocomial Tuberculosis:

- Early identification and rapid diagnostic work-up
- Prompt initiation of airborne precautions; remember respiratory procedures & therapy! Differs according to available resources
- Prompt initiation of anti-tuberculous drugs
- Monitor adequacy of therapy
- Staff screening and OHS issues
- Notification

Disease: African Tick-Bite Fever

- Rickettsial infections: R africae & R conorii
- Transmitted by ticks

... And many more ...
Disease: Malaria

- Travellers to endemic areas
- Airport malaria
- Runway malaria
- Taxi rank malaria
- NI: gloves (2001); multi-dose heparin vials (2000); IV therapy-apparatus, transfusions (1997); syringes (1950); laboratory-acquired

Disease: Malaria

- Nosocomial infection in South Africa:
  - NSI-related *Plasmodium falciparum* malaria resulting in death of a phlebotomy nurse in late 1990s. Source patient: confirmed *P. falciparum* malaria. Nurse: diagnosis initially missed; mismanaged when diagnosis eventually made; died ~3 weeks post NSI

Gram Positive South African bacterial foes:

**Staphylococci:**

- MRSA: 25% of 2815 patient’s blood cultures (Jan 1 - 31 Dec 2000, NASF); 34% of 2171 patient’s blood cultures (Jan - Dec 2001, NASF)
- vs. SENTRY study (AAC 2002 46(3):679-81); 46.4% of 84 patient’s blood cultures in 1998-9
- Mupirocin R: SENTRY (Tunridge J, et al. Poster 22512, 42nd AAC, 2002; California): 64% of 130 blood culture isolates
- hGISA: JH 2.9% of 175 isolates (first isolate described in 1998; SAMJ 2000; 90(11):1113; CHB 1.7% of 175 isolates; HJ 50% of 10 isolates)

**Opportunities:**

- *Bacillus spp*
  - *Paenicacillus popillae*:
    - 1998: RSA221 – clinical isolate with van A gene – MIC > 256 and 32 to vancomycin and teicoplanin respectively; but ORFs 1&2 from Tn 1546 absent from this isolate
- *B. lentus*:
  - 1999: RSA208 – none of the glycopeptide R determinants of *E. faecalis* detected
- *Corynebacterium spp*

Antimicrobial Misuse:

- Clonal spread of vanA and vanB strains within different hospitals
- Interhospital spread
- Persistence of one *E. faecium* vanA strain within hospitals

Spread Of Resistant Clones Of GRE

Out of Africa
Professor Adriano Duse, Johannesburg, South Africa
A Webber Training Teleclass

Spread Of Resistant Clones Of GRE

- Garden City 7-11
- Milpark 12-13,19
- JHB Gen 14
- Morningside 15
- Arewo 16-17
- Mulbarton 18

Challenges of reducing AMR:
QUALITY HEALTH CARE; ECONOMICS (VESTED INTERESTS); NATIONAL, GLOBAL CONCERNS ...
PREVENT TRANSMISSION  RESTRICT/OPTIMIZE USAGE  COMMUNITY
SURVEILLANCE: LOCAL, NATIONAL, GLOBAL
COSTING; EFFICACY; ACCOUNTABILITY/RESPONSIBILITY; RESEARCH

Gram Negative South African Bacterial Foes:
Enterobacteriaceae:

ESBL+ E coli: 3.7% of 1544 patient’s blood cultures (1 Jan – 31 Dec 2000, NASF); 2.4% of 1578 patient’s blood cultures (Jan Dec 2001, NASF) – vs. SENTRY study (Bell J, et al. Poster C2-314, 42nd ICAAC, 2002, California): 3.2% of 126 patient’s blood cultures in 1998-2001

ESBL+ Klebsiella: 15.2% of 1417 patient’s blood cultures (1 Jan – 31 Dec 2000, NASF); 32.4% of 1345 patient’s blood cultures (Jan Dec 2002, NASF) – vs. SENTRY study (Bell J, et al): 54% of 13 patient’s blood cultures in 2001

Enterobacter cloacae
ESBL Salmonella isangi, as discussed previously

Other Gram negatives:
Pseudomonas
Acinetobacter: Jan – March 2002, cluster of pan-R Acinetobacter baumanii detected. Phenotypically identical, but 2 genotypes on PFGE – 1 genotype on stethoscope and hands of HCW as well
De Jong, et al. Submitted to JHI

Approaches to Antimicrobial Resistance:
- Shorter courses, higher doses?
- Cyclic usage
- Prudent usage
- Education: prescriber, consumer
- Novel antimicrobial agents
- Novel therapeutic strategies:
  – Immunomodulation
  – Novel vaccines
  – Probiotic therapy
  – Improved technology esp. medical devices
- BACK TO THE BASICS: INFECTION CONTROL !!

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com
Gauteng’s hospitals of neglect

Disposal Of Waste:

Delivery of Sterile Supplies: Sterilization, Disinfection, and Waste Disposal:
Determining rates of NIs in South Africa:

- Nosocomial infection prevalence study
  - Initial pilot study to involve 2 academic, 2 non-academic provincial, and 2 private hospitals
  - Once potential problems identified and resolved, proceed with a strategy for a National Nosocomial Infection Prevalence Survey
- Study will look at major nosocomial infection categories to include: urinary tract, lower respiratory tract, bloodstream, & surgical site infections.
- NNIS/CDC HAI criteria used
- Method: training -> manual completion of appropriate questionnaires using NNIS/CDC definitions by trained personnel -> submission of these to Division of HEIC (NHLS & Wits School of Pathology) -> optical scanning of questionnaires -> capture of data into database (Formic) -> export of data into an appropriate statistical package e.g. Epi Info, SPSS -> analysis of data -> feedback; institutional confidentiality

Data collection form 1-General parameters:

- Patient demographics
- Medical risk factors
- Surgical risk factors & other invasive procedures
- Device-related risk factors
- Antibiotic and non-antibiotic therapy during admission

Surveillance:

- METHODS OF DATA COLLECTING AND ENTRY EMPLOYED IN THE SURVEYS
  - The Royal Hospitals Prevalence Survey 1995
  - Manual data recording
  - Completed questionnaires
  - Scanner
  - In-house database
  - Final analysis and report

Data collection forms 2 & 3:

- HAI–specific information
- Isolate information including AMR

Why automated data entry (ADE) using manual questionnaires & optical scanning?

- System accessible to all HCFs – once questionnaires completed, sent to centralized data processing unit → cost effective; rapid feedback
- Patient-based, not isolate-based
- ICN at cold interface; not in office / laboratory
- Improved speed & accuracy of data entry; substantial cost savings [Infect Control Hosp Epidemiol. 1997 Jul; 18(7):486-491]
  - 22-fold productivity increase cf. manual data entry (MDE) with validation
  - Saving of $ 0.63 (~ R 4.12) per questionnaire in clerical time
  - After validation, error rate of < 0.2 errors / 1000 responses (ADE) vs. 12.4 errors / 1000 responses (MDE)
Important considerations:

- Logistical hurdles – identification of data collectors (mandate from DoH), training, validation of training, funding, etc.
- Project will yield a CRUDE analysis of prevalence of HAIs – this is what DoH wants & requires. The critical importance of risk factor analysis in assessment of HAIs is fully acknowledged, but will have to be addressed – with more focused surveillance and fine-tuning – at a later stage.
- Motivator for infection control “political buy-in” from health authorities and administrators.
- Being a prevalence survey, results only represent a “snap-shot” of HAIs at one point in time.
- Hospital-wide surveillance will not be sustainable!
- As did the NNIS system in 1999, once the above objectives have been achieved, the hospital-wide approach must be dropped in favor of more focused (targeted), and comparable, surveillance components e.g. adult & pediatric ICU, surgical infections, high-risk nurseries.

Arguments for Alcoholic Hand Disinfection:
Rotter, ML.  JHI(2001)48(Suppl A): S4-S8

- Strongest and fastest activity against a broad spectrum of organisms
- More effective than soap and water in reducing the # of transient viable organisms on hands
- If well-formulated, less hand irritation and dryness than hand-washing with soap and water
- Economy in time of application
- Useful where water not available (rural areas)

Circumcision-related Sepsis:
- Outbreak of S pyogenes infections following ritual circumcisions
- Same razor blade used for multiple procedures
- Solution: agreement with Trad. Healer that sterile, single-use blades would be provided
- Outcome: no further cases

6. The Way Ahead For South Africa: A Land Of Contrasts:
- Back to basics !!
- Genetic requirement for "common sense"
- Practicable surveillance for NIs
- Waste disposal
- Re-defining the gold standard, with appropriate validations and risk-assessments
- Education; road shows
- Critically review screening of carriers; environmental IC issues
- Understanding culture and behaviours of those seeking alternative healers
- Control and monitoring of drug resistance (NASF)

AKNOWLEDGEMENTS:

Paul Webber
Prof H J Koornhof (Emeritus Professor, NHLS & Wits School of Pathology, SA)
Dr Adrian Britik (Head: Microbiology, AMPATH, SA)
Ms Jane Soester (IC Co-ordinator, Netcare Hospital Group, SA)
Mr P da Silva (research assistant) and ALL my Staff (CMD, NHLS & Wits School of Pathology, SA)
Mr M Hensher, DoH, South Africa
HISC in collaboration of DoH, Belfast, N Ireland
NSAF, CASA, DoH (SA)
GSH, JH, CHB H and Rob Ferreira H for their data

Thank you!